

VOLUME 7

*St. Louis Number*

NUMBER 5

---

THE  
MEDICAL CLINICS  
OF  
NORTH AMERICA

*MARCH, 1924*

PHILADELPHIA AND LONDON

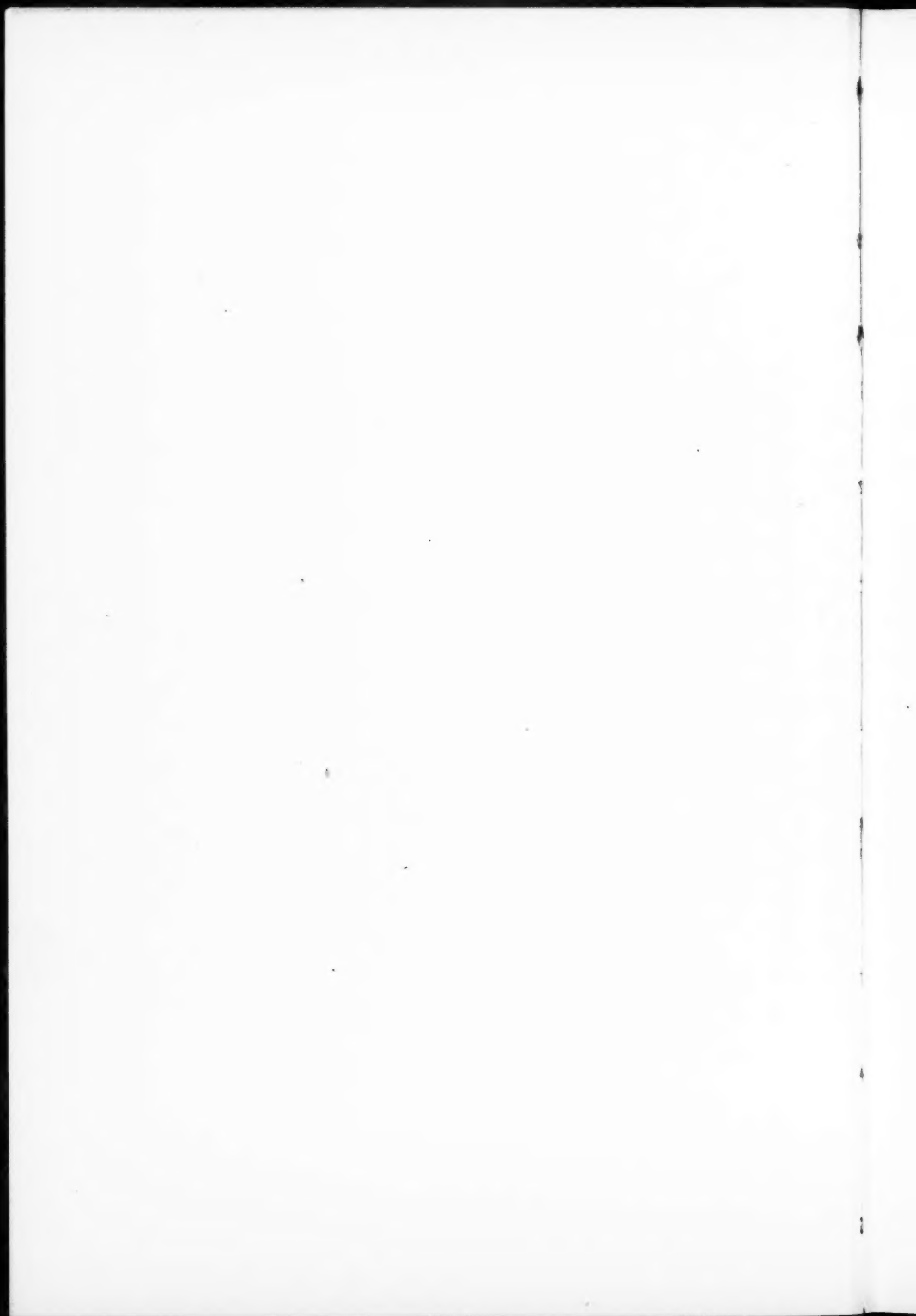
W. B. SAUNDERS COMPANY

---

COPYRIGHT, 1924. W. B. SAUNDERS COMPANY. ALL RIGHTS RESERVED

PUBLISHED BI-MONTHLY (SIX NUMBERS A YEAR), BY W. B. SAUNDERS COMPANY, WEST WASHINGTON  
SQUARE, PHILADELPHIA

MADE IN U. S. A.





## CONTRIBUTORS TO THIS NUMBER

---

**FRANCIS M. BARNES, Jr., M. D.,** Associate Professor of Nervous and Mental Diseases, St. Louis University School of Medicine; Neuropsychiatrist, St. Mary's Hospital; Consulting Neurologist, St. John's Hospital; Consulting Psychiatrist, St. Louis City Sanitarium.

**JULES M. BRADY, M. D.,** Associate Professor of Diseases of Children, St. Louis University School of Medicine; Physician in Chief, St. Ann's Infant Asylum.

**WILLIAM ENGELBACH, M. D.,** Professor of Clinical Medicine, St. Louis University School of Medicine; Chief of Staff, St. John's Hospital; Member of Staff, St. Louis City and St. Louis Maternity Hospitals.

**LOUIS HENRY HEMPELMANN, M. D.,** Instructor in Clinical Medicine, Washington University School of Medicine; Visiting Physician, Evangelical Deaconess Hospital.

**PHILIP C. JEANS, M. D.,** Associate Professor of Pediatrics, Washington University School of Medicine.

**RALPH A. KINSELLA, M. D.,** Associate Professor of Clinical Medicine and Acting Physician-in-Chief of Internal Medicine, Washington University School of Medicine.

**DREW LUTEN, M. D.,** Instructor in Clinical Medicine, Washington University School of Medicine; Assistant Physician, Barnes Hospital.

**J. CURTIS LYTHER, M. D.,** Associate Professor of Medicine, St. Louis University School of Medicine; Chief, Medical Service, St. Anthony's Hospital; Visiting Physician, St. Louis City Hospital.

**MCKIM MARRIOTT, M. D.,** Professor of Pediatrics and Dean, Washington University School of Medicine; Physician-in-Chief, St. Louis Children's Hospital.

**ALPHONSE McMAHON, M. D.,** Assistant in Medicine, St. Louis University School of Medicine; Assistant Physician, St. John's Hospital.

**CHARLES HUGH NEILSON, M. D.,** Professor of Medicine and Director of the Department, St. Louis University School of Medicine.

**WILLIAM H. OLMSTED, M. D.,** Associate in Medicine, Washington University School of Medicine.

**SIDNEY I. SCHWAB, M. D.,** Professor of Clinical Neurology, Washington University School of Medicine; Neurologist to Barnes, St. Louis Children's, and Jewish Hospitals; Chief of the Neurologic Clinic, Washington University Dispensary.

**HORACE W. SOPER, M. D.,** St. Louis, Missouri.

**ALBERT ERNST TAUSSIG, M. D.,** Associate Professor of Clinical Medicine, Washington University School of Medicine; Physician, Jewish Hospital; Assistant Physician, Barnes Hospital.

**JOHN L. TIERNEY, M. D.,** Instructor in Medicine, St. Louis University School of Medicine; Physician, St. John's and City Hospitals; Consulting Physician, Frisco Hospital.

**BORDEN S. VEEDER, M. D.,** Professor of Clinical Pediatrics, Washington University School of Medicine.

**GEORGE W. WILSON, M. D.,** Associate in Clinical Medicine, Washington University School of Medicine; Assistant Physician, Barnes Hospital.

**JOHN ZAHORSKY, M. D.,** Professor of Children's Diseases, St. Louis University School of Medicine; Attending Pediatrician, Bethesda Hospital, St. John's Hospital, and Baptist Sanitarium.

# CONTENTS

<b>Clinic of Dr. William Engelbach, St. John's Hospital</b>	PAGE
PITUITARY TUMOR.....	1365
<b>Clinic of Dr. Ralph A. Kinsella, Barnes Hospital</b>	
HYPERTENSION AND NEPHRITIS.....	1401
<b>Clinic of Dr. McKim Marriott, St. Louis Children's Hospital</b>	
NEPHRITIS IN CHILDREN.....	1413
<b>Clinic of Dr. Borden S. Veeder, Washington University School of Medicine</b>	
A DISCUSSION OF SOME OF THE DIAGNOSTIC PROBLEMS OF LOBAR PNEUMONIA IN CHILDREN	1421
<b>Clinic of Dr. Phillip C. Jeans, St. Louis Children's Hospital</b>	
DIPHTHERIA.....	1435
<b>Clinic of Dr. John Zahorsky, Bethesda Hospital</b>	
I. THE MOUTH-AND-HAND SYNKINESIA. II. ERYTHEMA NODOSUM IN AN INFANT. III. RECOVERY FROM EXTREME MARASMUS.....	1443
<b>Clinic of Dr. Jules M. Brady, St. Ann's Hospital</b>	
INTRACRANIAL HEMORRHAGE IN THE NEWBORN.....	1453
<b>Clinic of Dr. Sidney I. Schwab, Barnes Hospital</b>	
"HEART DISEASE" IN A NEUROLOGIC CLINIC.....	1461
<b>Clinic of Dr. Francis M. Barnes, Jr., From the Neuropsychiatric Division, St. Mary's Hospital</b>	
HYSTERIA.....	1481
<b>Clinic of Dr. John L. Tierney, St. John's Hospital</b>	
HEADACHE.....	1515
<b>Clinic of Dr. Albert Ernst Taussig, From the Medical Service of the Jewish Hospital</b>	
NON-DIABETIC GLYCOSURIA AND NON-GLYCOSURIC DIABETES.....	1545
<b>Clinic of Dr. George W. Wilson, Barnes Hospital</b>	
INFLUENZA.....	1553
<b>Clinic of Dr. J. Curtis Lyter, St. Anthony's Hospital</b>	
MULTIPLE ADENOCARCINOMA OF THE BRAIN.....	1583
MULTIPLE EMBOLI.....	1593
PERFORATING GASTRIC ULCER.....	1601
<b>Clinic of Dr. Drew Luten, Barnes Hospital</b>	
ON THE USE OF DIGITALIS IN THE TREATMENT OF PATIENTS WITH DIFFERENT TYPES OF HEART DISEASE.....	1607
<b>Clinic of Dr. Horace W. Soper, St. Luke's Hospital</b>	
BENIGN PYLORIC OBSTRUCTION IN THE AGED.....	1621
<b>Metabolism Clinic of Dr. William H. Olmsted, Barnes Hospital</b>	
THE VALUE OF WEIGHT CURVES IN DETERMINING THE SEVERITY OF DIABETES.....	1631
<b>Clinic of Dr. Alphonse McMahon, St. John's Hospital</b>	
PURPURA.....	1645
<b>Clinic of Dr. Louis Henry Hempelmann, Evangelical Deaconess Hospital</b>	
MIKULIC'S DISEASE.....	1663
<b>Clinic of Dr. Charles Hugh Neilson, St. Louis University</b>	
FOCAL INFECTION IN GENERAL, WITH SPECIAL REFERENCE TO THE PROSTATE.....	1669

# THE MEDICAL CLINICS OF NORTH AMERICA

---

---

Volume 7

Number 5

---

---

CLINIC OF DR. WILLIAM ENGELBACH

ST. JOHN'S HOSPITAL

---

## PITUITARY TUMOR

**Variation of Recent from Text Description of Pituitary Neoplasm. Incidence as Compared with Pituitary Disorders. Newer Pathogenesis. Evaluation of Sellar Deformity and Ocular Signs. Pituitary Headache. Hormonic Signs. Diagnosis of Progress of Tumor Growth. Indications for Treatment.**

A VARIANCE from the present-day conception of pituitary neoplasm as derived from authoritative texts and recent medical literature led to the choice of this entity as the subject for this clinic. The re-analysis of 13 cases, some of which have been under personal observance for from one to ten years, presented many points incongruous with the present-day teaching. The incidence of these tumors compared with the general group of pituitary disorders; the importance of the sellar deformity, always stressed as the most positive diagnostic sign; the great variability of the ocular signs from the ordinarily accepted temporal hemianopsia; the unusually prolonged course, with intervals of progression and recession in the tumor growth, presenting at various times a series of kaleidoscopic clinical pictures, are features derived from studies of these tumefactions. Furthermore, the experience of long observation of these cases has diverted the diagnosis from the mere presence of a pituitary tumor to the growth progression of that tumor. It is this evidence of progressive, stationary, or regressive growth in these tumors which indicates their prognosis and treatment.

TABLE I

No.	Name, sex, age.	Gen-eral No.	Neighborhood signs.					General intracranial pressure signs.	Progression of tumor growth.	Hormone signs.	Etiology.
			Sella.	Ocular signs.			N. III, IV, VI.				
				Perimeter.	Fundus.						
1	J. N. (M.). Aged 14. Dur., 4 yrs.	748	Greatly enlarged, 19 x 26 mm.	Not obtainable (blind- ness).	Bilat. neuroretinitis, blindness.	N. III and VI involved. P. unequal, rt. larger.		Neuroretinitis, headache, vom- iting (without nausea)	Marked, death in 1 yr.	Polyuria, overgrowth of osse- ous system. No obesity.	Trauma.
2	H. A. T. (M.). Aged 33. Dur., 14 yrs.	1622	18 x 25 mm. P. proc. and a. wall eroded.	Homonymous hemianop- sia (early).	Optic atrophy, rt. and left.	N. negative. P. equal, rt. negative to light, left, slow.		Headache, final optic atrophy, papillary changes.	Constant 3 yrs. Absent 3 yrs. Present last 2 yrs. Stationary since opera- tion.	Polyuria, polydipsia, polypha- gia, myalgias, alternation, loss of libido and potency. No obesity.	Typoid.
3	T. S. (M.). Aged 39. Dur., 10 yrs.	3708	17 x 25 mm. P. proc. eroded.	Bilat. contraction.	Negative. Rt. 20/32. Left 20/19.	N. negative. P. unequal, left negative to light, rt. slow.		Headache, vertigo, deafness, tinnitus. Nausea and vomit- ing (initial). No choked disk.	Absent 4 mos. No in- crease in general or neighborhood signs.	Acromegaly, polyuria. B. M. R., +19%. Picturine nega- tive. Adrenalin negative.	Cranial trauma (?).
4	H. A. L. (M.). Aged 30. Dur., 8 yrs.	757	18 x 28 mm. A. and p. proc. eroded.	Negative (Wolfer).	Normal until late stage (Wolfer).	N. negative. P. equal.		Headache, vertigo, facial twitching (?). No choked disk.	Rapid progression signs.	Motor weakness of rt. arm. Obesity.	Negative.
5	T. L. (F.). Aged 40. Dur., 6 mos. (from history, now 1 yr.)	3822	12 x 22 mm. A. and p. proc. eroded.	Temporal hemianopsia (complete left, partial rt.). Bilat. contraction.	Temporal sides pale, choked disk negative.	N. negative. P. equal.		No headache, choked disk negative.	Initial symptom, amenor- rhea (7 yrs.). Growing tumor, 1 yr.	Amenorrhea, hypoglycemia (0.24-0.27%), obesity. No polyuria or glycosuria. B. M. R., -2%.	Early hypopituitarism (menopausal, aged 35-41). Tumor symptoms devel- oping 6 mos. previous to observation.
6	A. H. L. (F.). Aged 47. Dur., 2 yrs.	2998	12 x 14 mm. P. proc. eroded.	Unilat. hemianopsia (rt.); late bitemporal.	Atrophy rt. optic, pallor left disk.	N. negative. P. equal.		Headache, atrophy rt. disk, pulsation in left ear.	Gradual progression last year.	Obesity, irregular menses, ne- orrhagia, amenorrhea.	Suspect leuc.
7	E. W. P. (M.). Aged 37. Dur., 3 yrs.	3813	7 x 17 mm. A. and p. proc. eroded.	Not obtained.	Not obtained.	N. negative. P. unequal, rt. larger; both slow to light.		Blurring of vision.	Absence of progress. Death from pulmonary infarction.	Polyuria, polydipsia, polypha- gia, glycosuria, hypertensi- on, impotency and loss of libido, pigmentation, hypothyroid- ism (initial). B. M. R., -19%. Picturine negative. Adrenalin negative.	Not obtainable.

8	F. E. (M.). Aged 35. Dur., 1½ yr.	3873	13 x 16 mm. No erosion.	Contraction in rt. eye, less marked in left.	Negative. O. D. 20/19. O. S. 20/19. Hypermetropia, 1½ D.	N. negative. P. equal.	Negative.	Absent 2 yrs.	Polyuria, polydipsia, glycosuria, hibernation, obesity, dyspnea, rigide crampa. B. M. R., +35%. P. negative. Adren. positive.	Typhoid and heredity.
9	J. E. G. (F.). Aged 47. Dur., 10 yrs.	1328	10 x 15 mm. P. proc. eroded.	Progressive left opp. quad. hemianopia. Gen'l contraction, left; rt. negative.	Simple optic atrophy, left disk.	N. negative. Left pupil slow to light.	Intermittent headaches, left optic atrophy, facial neuralgia.	Progressive hemianopia in left eye, not relieved by artificial menopause (x-ray).	Overgrowth of osseous system. No signs of posterior lobe involvement. B. M. R., +8%.	Pregnancy.
10	C. S. (M.). Aged 18. Dur., 3 yrs.	624	Largo, not abn. normal. 8 x 13 mm.	.....	.....	N. negative. P. equal. react to light and accommodation.	No headaches or ocular symptoms.	Constant until death (due to hypoadrenia and acidosis).	Pituitary glycosuria, eunuchoid stigmata (no obesity). Four-plus Wassermann (no reaction to treatment).	Lues.
11	M. E. S. (F.). Aged 38. Dur., 6 yrs.	3119	Normal size.	Homonymous hemianopia. All eye symptoms cleared up under decompression operation and mild treatment.	Incipient optic atrophy.	N. negative. P. equal. react normally.	Transient facial paralysis (two days timula, headache after decompression, right school for 3 yrs. after decompression (very normal)).	Constant until decompression.	Change in periods at 30, gradual decrease until amenorrhea at 35. Mild changes in uterus. Late tendency to obesity (after 40).	No etiologic factors in history. Response to antihypertensive treatment. No decompression operation.
12	B. T. (F.). Aged 34. Dur., 5 yrs.	899	Normal size.	Normal for white. Homonymous hemianopia at one time.	Bilat. papilledema. Retina pale. Blurring of arteries.	N. negative. P. equal.	Severe headaches, syncope, attacks, nausea and vomiting, disk changes.	Practically none.	Intermittent polyuria, with oliguria.	Lues.

**Incidence.**—We have been led to believe, first, that pituitary tumor is the most frequent cause of pituitary disorder, and, second, that unless the signs of pituitary tumor are present, such disorder cannot be diagnosticated. Contrary to this opinion relative to their incidence, it has been the experience of the writer that they occur very infrequently as compared with the total number of pituitary disorders. Furthermore, if *only* those cases presenting neighborhood and general intracranial signs of pituitary neoplasm were accepted as positive pituitary disorders, more than 95 per cent. of pituitary diseases would be unrecognized. In a total of 147 pituitary cases collected up to 1920, only 8, or 6 per cent., were due to pituitary neoplasm. Since that time, in an additional number of 228 pituitary disorders, only 5 more tumors have been observed. In this series of 375 uncomplicated pituitary disorders, tumor was the cause in only 13 cases, less than 4 per cent. of the total. This emphasizes the fact that, while the signs for pituitary tumor when present are important in diagnosis, yet their absence in over 95 per cent. of the pituitary cases places them as relatively insignificant in value. This fact alone should help to prove that we are far beyond the stage of pituitary tumor as the only means of determining and interpreting pituitary disorder. On the contrary, it has been found that the general hormonal signs are very much more dependable for the diagnosis of secretory disturbances of the hypophysis than the neighborhood and general intracranial symptoms upon which the diagnosis of neoplasm of this gland is made. This is true because the general hormonal signs are present in the great majority of cases of pituitary disorder, whether that disorder is due to tumor of the gland or to a simple disturbance of its function.

**Etiology.**—The etiology of the so-called pituitary syndromes is yet under considerable dispute. The French school, led by Camus and Roussy, contend that any lesion of the hypothalamus or interpeduncular region in the neighborhood of the hypophysis could and frequently does produce these clinical complexes. The followers of this school maintain that even the symptomatology

of pituitary tumor is derived from pressure upon other structures in the neighborhood of the hypophysis, instead of being due to disordered secretion or function of the gland itself. Bailey and Bremer have recently supported this hypothesis. They review the literature confirming these ideas and, in addition, report some personal experiments substantiating these clinical results. The most important proof they offer is experiment upon dog No. 10, in which injury was done to the hypothalamic region, producing a complete pituitary syndrome, including the typical

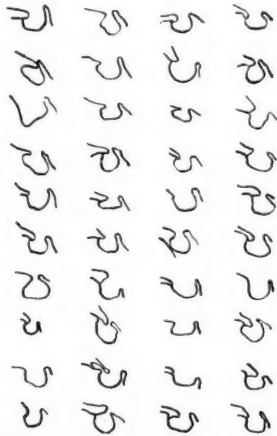


Fig. 239.—Variations in size and shape of the *normal* sella turcica. (From Dr. H. S. Howe's Normal and Abnormal Variations in the Pituitary Fossa, Neurological Bulletin, Vol. 2, June, 1919, p. 233.)

adiposity. At autopsy the hypophysis in this animal (No. 10) was found to be absolutely normal. Their investigations, however, did not include the mass of evidence (anatomic, clinical, and surgical) bearing upon the direct secretory and functional disturbances of the pituitary as etiology for these clinical pictures. They also failed to take into consideration such recent work as that of Evans and Smith, of the University of California, who have proved experimentally that the secretion from the anterior lobe actually does produce osseous and genital changes, whereas that from the posterior lobe objectively influences the

deposition of fat. That in two species (tadpoles and rats) these changes of bone could not be due to trauma or any other effect upon the hypothalamic or interpeduncular region was beyond question. During the metamorphosis of these species (amphibian and rodent), at which time these experiments were being made, this part of the brain was so far removed from the hypophysis that it could not have been injured by these experiments directed toward the pituitary. Aschner (1912) maintained that he had experimental proof that these syndromes, with the exception of adiposity, were due to lesion of the tuber

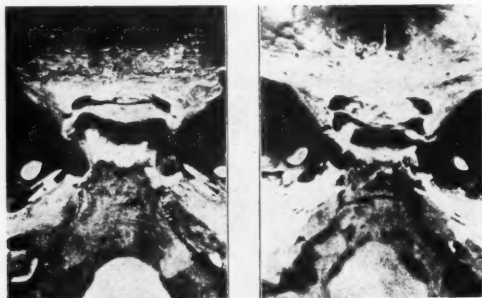


Fig. 240.—Left: A normal sella showing the relation of the anterior clinoid process to the pituitary fossa. Note the median position of the fossa. Right: A normal sella having the anterior, middle, and posterior clinoid processes on the left, and the anterior and middle on the right, connected by a bony spicule, which does not materially change the size of the pituitary gland within these processes. (From Dr. H. S. Howe's article.)

cinereum. The location of the lesions causing the typical girdle adiposity in the pituitary syndrome of Froehlich has been given in as widely separated parts of the nervous system as the cerebrum to the nerve endings in the individual cells involved. A. Biedl, for instance, describes such obesities as a sequence to cerebral lesions. J. Bauer, on the other hand, inclines to ascribe the pathogenesis of all adiposities to chromosomal insufficiency, due to primary defects in the germinal gamete, and thus relates them to inherent properties of the individual involved cells.

There is also considerable evidence presented by the anatomic and surgical pituitary lesions, as well as the therapeutic



effect of pituitary substances upon the symptomatology of these disorders, supporting the inference that the lesion or disturbance of function must be located in the hypophysis itself, and not in any of the surrounding brain tissue or distant body cells. Kenneway and Mottram have analyzed the data pro and con on this problem in diabetes insipidus, and have concluded that the relationship between actual lesions of the hypophysis and this disease is certainly more than casual. They state that there is no convincing evidence that lesions in the neighborhood of the hypophysis will consistently produce this condition. The absence of pathologic changes noted in the neighborhood tissue of small pituitary tumors and in the large number of



FIG. 6.

ACP Anterior clinoid process.  
DS Dorsum sella.  
F Floor of sella.  
OP Orbital plane.  
OS Optic sulcus.

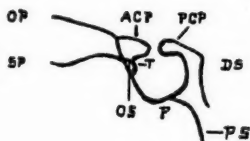


FIG. 7.

PCP Posterior clinoid process.  
PS Posterior wall of sphenoidal sinus.  
SP Sphenoidal plane.  
T Tuberculum sellae or olivary process.

Fig. 241.—Silhouettes of two normal sellas as they are projected by the x-ray. Note the tuberculum or olivary process (T) which forms the antero-superior boundary of the fossa. (From Dr. H. S. Howe's article.)

aneoplastic pituitary syndromes in the human tends to contradict the experimental work of physiologists. The well-known therapeutic effect of the injection of the extract of the posterior lobe of the hypophysis in controlling diabetes insipidus is one of the most important arguments against a basilar cerebral lesion as a cause for this condition. If the lesion were not located in the hypophysis and due to a disorder of its function, this substance certainly would have no effect in relieving the polyuria, its most distressing symptom. Another argument favoring the pituitary cause of these symptom-complexes is that many other general signs specific of hypophyseal disorder, such as osseous changes, menstrual disturbances, etc., are found present in the majority of these entities. While this question is far

from settlement, the trend of opinion of many clinicians and pathologists seems to favor the glandular origin; whereas the physiologists and many surgical experimenters contend that simple pituitary disorder does not account for these various so-called pituitary syndromes.

The probable etiology of the neoplasm in these 13 cases is as follows: Two immediately followed typhoid fever, 3 were associated with positive lues, and 1 with suspected lues, 2 followed within a short time a very severe cranial trauma, and 1 began during pregnancy. In 4 no definite infectious, traumatic, or familial etiology was obtainable. It is well known that typhoid



Fig. 242.—Sella, Case II. Note the enormous size, 18 x 25 mm. (normal maximum measurements 10 x 15 mm.), with erosion of the posterior clinoid process and self-decompression into the sphenoid cells anteriorly.

is particularly influential as an etiologic factor in this condition. Cushing, Messedaglia, and Chanal have referred to a typhoid infection preceding these neoplasms. Cushing also reports a very classical case of gumma of the hypophysis, controlled by autopsy, which had gone through hospital observation and was discharged as a case of diabetes mellitus. Lues seems to be an unusual factor in our small series of cases. It is also interesting to note in these luetic cases that 2 had no enlargement of the sella turcica, yet had sufficient other symptomatology, such as other neighborhood and intracranial pressure signs, to indicate that the lesion was most probably in the pituitary gland. In one of these 2 cases, besides these intracranial pressure symptoms, the patient had

other general hormonal signs, such as polyuria, which reacted to pituitary treatment, some confirmation that the hypophysis was involved in the production of this lesion. Oppenheim has reported a large number of cases of specific basal meningitis, however, which have had some hypophyseal symptoms, such as glycosuria or diabetes insipidus complexes. In one of our cases (No. 11) there was a marked response to specific treatment following simple temporal decompression operation, the patient regaining complete normal vision after having had for a number of months homonymous hemianopsia and incipient

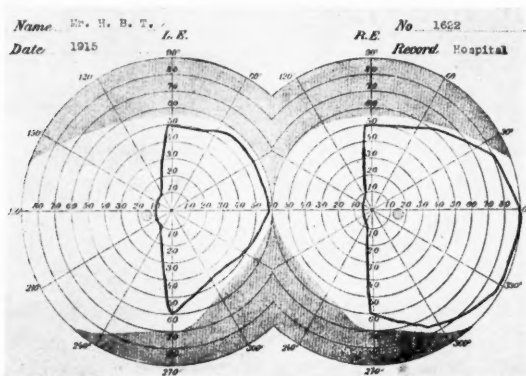


Fig. 243.—Perimeter chart, Case II. Note the classical homonymous hemianopsia. (Dr. H. S. Hughes, St. Louis.)

optic atrophy. Another of the luetic cases (No. 10) had as its chief complaint a glycosuria, which responded temporarily to antispecific treatment. In 3 of these cases having a luetic etiology (Nos. 10, 11, and 12) there was absence of an abnormally enlarged sella.

**Symptomatology.**—The symptomatology of pituitary neoplasm has been described with so much detail that we will take up only those points dealing with exceptions to the earlier descriptions. The symptomatology can be readily subdivided into (I) those symptoms produced by intracranial pressure and (II) those due to the effect of the hormones of the hypophysis

upon other structures and distant organs of the body (hormonic signs). (I) The intracranial pressure symptoms can again be subdivided into (1) neighborhood or localized signs, due to pressure upon the tissues in the region of the pituitary gland, and (2) general intracranial pressure symptoms, resulting from increased pressure within the cranium. (II) The hormonic signs are regrouped into (1) general hormonic signs, affecting the individual as a whole, such as height, weight, proportions, adiposity, pigmentations, hair growth, etc.; (2) regional hor-



Fig. 244.—Sella, Case III. Enormous enlargement (17 x 25 mm.), with erosion of the posterior clinoid process.

monic signs, which are the changes in local or limited portions of the body, as of the nose, lips, teeth, mammae, genitalia, fingers, toes, etc.; and (3) laboratory signs, which are really a part of the general hormonic signs, but are classed under a different heading on account of the special technic required for their identification. These laboratory signs consist of changes in the basal metabolism and blood chemistry and the effects of the injection of various pituitary substances upon the blood-pressure, pulse-rate, color, involuntary muscle contractions, urinary output, etc.

The neighborhood or localized intracranial pressure symptoms are unquestionably the most important with regard to both diagnosis and treatment of pituitary struma. Yet early descriptions of these signs have been so dogmatic that they have been misleading, on account of overrating their importance and frequency of occurrence. This has actually prevented the recognition of a great many pituitary disorders in which they were absent. As previously stated, the neighborhood pituitary signs are of value only in those pituitary disorders having a pituitary neoplasm as their etiology, and even in a small percentage of these cases some of the cardinal signs, such as

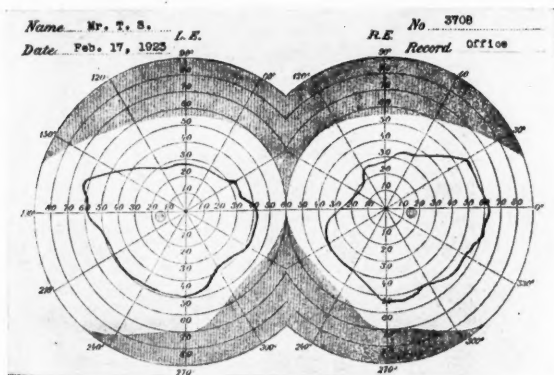


Fig. 245.—Perimeter fields, Case III. Note the only moderate bilateral paracentral contraction to form fields. (Drs. North and Jones, St. Louis.)

enlargement of the sella or changes in the perimeter readings, are absent. Surgeons particularly are very apt to place entirely too much credence in neighborhood signs as positive diagnostic evidence of pituitary disorder, and to be inclined to exclude the hypophysis in all cases in which neighborhood signs fail to appear. This is due to the fact that it is not generally known that about 95 per cent. of the typical pituitary disorders are due to causes other than tumor of the hypophysis, consequently this large percentage would go unrecognized if evidence pointing to pituitary struma were necessary for their diagnosis.

The *deformity or erosion of the sella turcica* is the one sign which has obsessed the diagnostician in ferreting out a possible pituitary cause for the classical syndrome. We are convinced that the variations in size of the sella within the normal are so great that many cases are misjudged, both as to an abnormally small sella and as to a pathologically large sella. When one considers Fig. 239, it is easy to realize the marked variation in the sella turcica appearing in normal individuals at various ages. While Keith's measurements of 9 x 14 mm. and Cush-



Fig. 246.—Sella, Case IV. Note the enormous enlargement (18 x 28 mm.), with erosion of the anterior and posterior clinoid processes.

ing's measurements of 10 x 15 mm. as the maximum size of the normal sella are good general guides, some variations from these, depending upon the size of the skull, sinuses, etc., must be allowed. A small, imprisoned sella, in which the anterior and posterior clinoid processes apparently are closely approximated, is considered by some authorities to indicate an abnormally decreased size of the hypophysis. An anatomic study of the pituitary fossa as related to the anterior and posterior clinoid processes and the sellar tubercle, as shown in Figs. 240, 241,

demonstrates the fact that this excavation is really not modified by the clinoid processes, which are located at least 4 to 6 mm. lateral to this fossa. These show how the anterior and posterior clinoid processes could be approximated without producing any impingement upon the infundibulum or the pituitary gland, which lie this distance within these processes. There is no intention to deny the absolute value of a very large or eroded sella as evidence of a pituitary tumor, but it is necessary to appreciate the fact that pituitary tumors can and occasionally do exist without modifying the normal size and shape



Fig. 247.—Sella, Case V. Large, measuring 12 x 22 mm. Erosion of the anterior and posterior clinoid processes.

of this bony saddle. This occurs very early in the course of pituitary tumor and in those tumors in which the growth might be directly upward between and within the anterior and posterior clinoid processes, or directed laterally without producing any enlargement anteriorly or posteriorly of the silhouette of the sella as obtained upon the roentgenogram.

In these 13 cases there were 4 in which there was no definite enlargement of the sella turcica, and 3 in which there was absolutely no enlargement or erosion of any part of the sella portrayed by the radiogram. In all these cases there was some

tumefaction of the pituitary as shown by the neighborhood signs, such as defects in the perimeter markings or other ocular symptoms, associated with the general hormonal signs, as complete amenorrhea, polyuria, localized pituitary obesity, specific osseous changes, etc. In some of the others a normal sella for a considerable length of time was demonstrated. Sooner or later, in the majority, erosion of either of the processes or enlargement of the sella occurred. These objective signs would force one to believe that in a certain percentage of cases tumor of this gland can exist for a time, at least, without

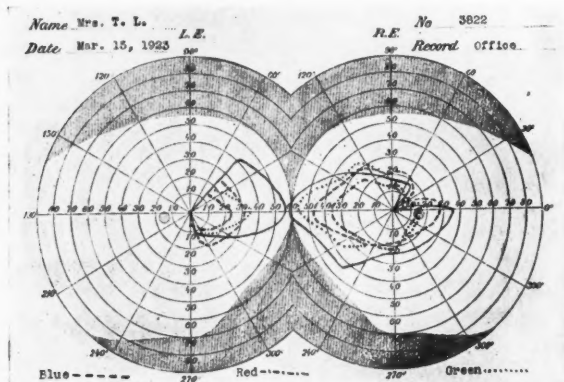


Fig. 248.—Perimeter fields, Case V. Note the marked bilateral contraction to both form and color fields. Complete temporal hemianopsia on the left, partial on the right. (Dr. C. G. Beall, Fort Wayne, Ind.)

any localized changes in the sella turcica as obtained by the roentgenogram. The most interesting and striking case of this kind is No. 11, a young unmarried school teacher, whom we were treating for a number of years for aneoplastic hypopituitarism of the anterior lobe, having had the characteristic amenorrhea for two years, associated with chloasma and a normal sella. While under observation, two years after the onset of the amenorrhea, she suddenly developed a homonymous hemianopsia and a primary atrophy of the optic disk. For this she was operated upon, an exploration of all the sinuses



first being made, without benefit to the eye symptoms, and then a temporal decompression was done, with partial relief of her hemianopsia and primary optic atrophy. Soon after operation she also developed a transient paralysis of the seventh nerve, lasting two days, from which she recovered entirely. Although she had no history or signs of lues, she was then put upon antispecific treatment. Without other operative procedure she then recovered completely as far as any intracranial symptoms were concerned. Her sight returned to normal and the



Fig. 249.—Sella, Case VI (taken October 4, 1921). Very slight enlargement, measuring 12 x 14 mm. Erosion of the posterior clinoid process.

so-called optic atrophy disappeared entirely, so as to allow her to return to teaching, which she has continued for the past three years. Her amenorrhea and pigmentation, however, were not affected throughout the entire course. During this time frequent pictures were taken of the sella turcica, and at no time was there found any change from a practically normal sella which she had had from the very beginning, three years before operation.

In 2 other cases that we have reported herewith (Nos. 10 and 12) there was also absence of enlargement of the sella,

although ocular and other neighborhood signs were present, which would tend to localize the lesions in the hypophysis. Both of these cases had general hormonal signs, such as polyuria, glycosuria, and osseous and other changes indicative of pituitary disorder. The prolonged observation in these cases has convinced us that a normal-sized sella is not contradictory to the possibility of pituitary tumor, 4 of our cases (30 per cent.) having had normal-sized sellas. It is now well known that an unusually small or a normal-sized sella does not preclude



Fig. 250.—Sella, Case VI (taken November 21, 1923). Slight increase in size over Fig. 249, measuring 9 x 21 mm.

the possibility of pituitary secretory or functional disorder, because in these cases over 95 per cent. have such sellas and yet present very positive evidence of pituitary disorder.

The next most abused neighborhood signs with regard to its importance in the diagnosis of pituitary tumor are the *ocular signs*. The old idea of bitemporal hemianopsia as a necessary sign of pituitary tumor has been so indelibly fixed in the medical mind that even the special knowledge of the oculist and the neurologic surgeon has not appreciated the fact that it is probably one of the rarer perimeter signs produced by these tumors.

On the other hand, the classical blindness or perimeter defect varies so much from this that, when it is found, it is usually

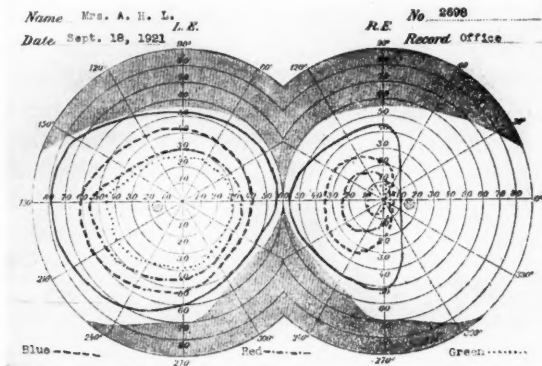


Fig. 251.—Perimeter fields, Case VI (September 18, 1921, by Dr. E. F. Krug, New York). Unilateral hemianopsia, temporal portion of the right eye (left normal).

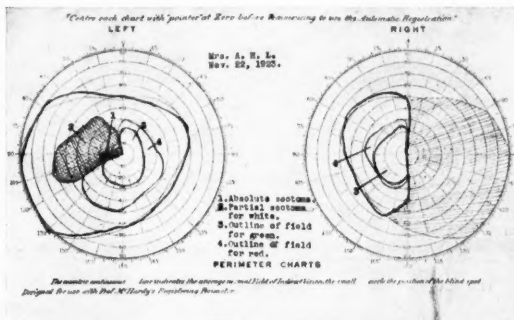


Fig. 252.—Perimeter fields, Case VI (November 22, 1923, by Drs. Wolfner and Wiener, St. Louis). Almost complete bilateral hemianopsia. The right eye is practically the same as in Fig. 251. The left eye, which previously was normal, now shows (1) absolute scotoma, (2) partial scotoma for white, (3) concentric constriction of the field for green, (4) reduced central constriction of the field for red, and (5) almost complete temporal hemianopsia for form.

attributed to some other condition, such as hysteric blindness, toxic amblyopia, or infection secondary to some focal lesion,

as sinusitis. Our experience with this series of neoplasms has confirmed that of others who have studied larger series for a prolonged time, that a *transient, fleeting blindness*, asymmetric and varying in its location, is the more constant ocular sign of these tumors. This retinal blindness is due, of course, to direct or dragging pressure upon the chiasm or the optic tract just posterior to the chiasm. The amount of retina involved depends upon the location of the pressure, and, in consequence, upon the direction of the growth of the tumor. Should a tumor grow directly anteriorly and press directly upon the chiasmic fibers where they cross, then a typical nasal blindness, which

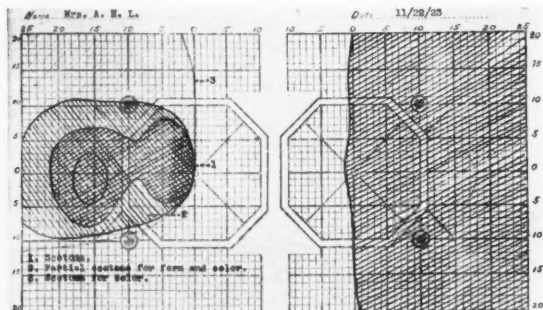


Fig. 253.—Case VI, Lloyd's stereocampimeter chart (November 22, 1923, by Drs. Wolfner and Wiener). Right eye: temporal hemianopsia. Left eye: (1) scotoma; (2) partial scotoma for form and color; (3) scotoma for color.

produces a bitemporal hemianopsia, occurs. This phenomenon, however, happens very rarely with these tumors. The tumor frequently grows laterally and produces pressure or dragging upon the mesial fibers of one optic tract. This produces a nasal retinal blindness in the opposite eye, with a temporal defect of the retina of the eye of the same side. The amount of blindness produced depends entirely upon the number of fibers involved. It may be a very small point or may involve the complete half of the eye, or it may produce obliterating blindness of the entire optic tract and cause homonymous hemianopsia, with nasal blindness in one eye and temporal blindness in the other. As

the tumor grows, it sometimes decompresses the anterior wall of the sella (the posterior wall of the sphenoid cells) or breaks through the posterior clinoid process. When this self-decompression occurs, the pressure is temporarily relieved from various portions of the optic chiasm, allowing the sight to return to the retina supplied by those fibers. This decompression and release of pressure upon the optic tract or chiasm or its fibers accounts for the very peculiar course in relief from or change in the eye symptoms of the patient. For example, at one time there may be a small blind-spot in one portion of the periphery of one eye, and later this may be gone entirely, with complete blindness of one-half of the opposite eye. Again, in a short time afterward this unilateral hemianopsia may disappear entirely, and there may be a complete blindness of the opposite eye. These variations of blindness during the course of the disease have misled oculists to believe it to be due to causes other than neoplasm. In our series of cases Nos. 2 and 12 are outstanding examples of these misinterpretations. Another very common error in these cases is the suspected diagnosis of lesion posterior to the chiasm, such as cerebellar or occipital lobe tumor, especially in the cases having homonymous hemianopsia. Indeed, this diagnosis had been made in 2 of these cases by very competent neurologic surgeons, one of whom forwarded a signed statement, with the information that this perimeter reading (homonymous hemianopsia) was never found in pituitary tumor. It will be noted that No. 2, in which case the diagnosis was confirmed at operation, had such a classical finding, as well as No. 11, also a very typical case of this kind, which finally recovered completely from both the homonymous hemianopsia and the so-called optic atrophy. Mistakes in the diagnosis of localization of these tumors having homonymous hemianopsia can to some extent be obviated by considering the pupillary reflex and the central blindness involving the macula lutea.

The perimeter and other ocular signs are of prime importance as indicators of the progression of growth of the tumor. Yet, on account of the fleeting character of the blindness, due to the self-decompression of the tumor, one should not be misled by the

ocular findings. For instance, in some of the cases the ocular findings temporarily clear up during the most marked progression of growth of the tumor. In these instances the perimeter blindness changes because the decompression temporarily relieves the pressure upon the optic chiasm or tract. For this reason, other neighborhood signs, such as increased size and erosion of the sella turcica, as well as pressure upon other structures in the neighborhood and the general intracranial pressure symptoms, should be taken into consideration, in order properly

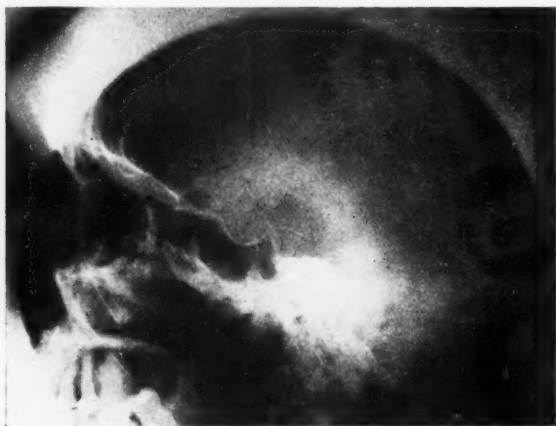


Fig. 254.—Sella, Case VII. Considerable enlargement, 7 x 17 mm. Erosion of the anterior and posterior clinoid processes.

to estimate the progression or regression in size of the neoplasm. Number 6 is a typical example of a progressive tumor, going from a unilateral partial hemianopsia to a rather classical bitemporal hemianopsia in two years. During this time there was a marked enlargement in the sella (Figs. 249, 250), from 14 to 21 mm. in the anteroposterior diameter, the vertical depth decreasing from 12 to 9 mm. due to excavation under the anterior clinoid process. Diplopia and bilateral optic atrophy were present in this case, with only very mild, transient headaches without other general intracranial pressure symptoms. An illustration of a

unilateral perimeter defect is shown in Case 9 (Figs. 257-259), demonstrating a progression of pressure upon the optic nerve probably anterior to the chiasm. This blindness began in the lower temporal field of one eye and gradually spread upward. Thus far the other eye has not been involved. Case 3, on the contrary, presents a rather common variety of the course of these strumas. It had a progressive tumor, which ceased growing and remained stationary for many months. In this case all general intracranial symptoms, as headache, photophobia, vomiting, etc., have disappeared and remained absent. There



Fig. 255.—Sella, Case VIII. Slightly enlarged, measuring 13 x 16 mm.

has been no change in sellar deformity or ocular signs on serial observations. We have not found the inversion of the color fields of much significance in this series of cases, due to the fact that the majority of them were first observed at a comparatively late stage. Lillie has stressed the clinical significance of careful color perimeter examination, especially in suspect early cases. He placed as much importance in the early defect of the color field as in form defect. The first deviation from the normal he found was scotoma, in the form of enlargement of the physiologic blind-spot, usually toward the upper temporal quadrant.

DeSchweinitz has confirmed Traquair's original description that the deviation from form of the perimeter periphery progresses around the center "clockwise in the right field and counter-clockwise in the left." He reaffirms Lillie's experience that it is probable that the earliest changes are extensions from the physiologic blind-spot. He declares further that many deviations from these paracentral scotomata and symmetric bilateral types of amaurosis occur during different stages of a progressive tumor. Hence, many exceptions to these classical distortions of the visual fields are presented, and the changes are found to be

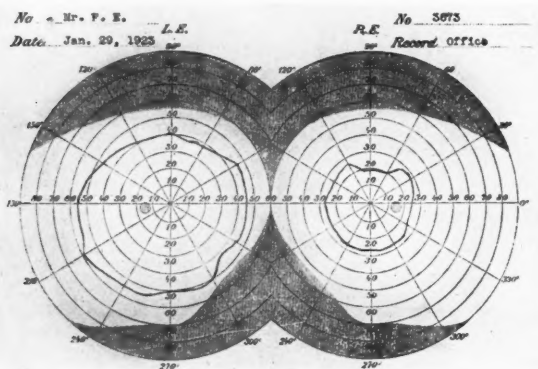


Fig. 256.—Perimeter fields, Case VIII. Paracentral contraction of form fields, more marked on the right. (Drs. North and Jones, St. Louis.)

unilateral almost as often as bilateral, and homonymous changes appear almost as frequently as bitemporal hemianopsia. Lillie reports 4 normal perimeter fields in a series of 42 positive pituitary strumas.

Other ocular signs, such as choked disk, optic atrophy, and eye muscle paralysis, are of less importance than the perimeter markings as to the diagnosis of tumor and the localization of the same. The involvement of the third, fourth, and sixth nerves is a late sign, rarely occurring in beginning tumor or gumma of the hypophysis. Choked disk is one of the signs of general intracranial pressure, present with a tumor or any other disease



producing such change. It may for this reason follow a previous optic atrophy of the disk. It has no significance with regard to localizing the process in the pituitary gland.

Primary optic atrophy was present in 4 of this series, neuroretinitis in 1, and choked disk in 1. In 4 cases the oculist reported no abnormal findings about the disk, and in 3 cases the fundus was not examined. Paresis of the third, fourth, or sixth nerve occurred in only 1 of the cases. The pupils were unequal in 3 cases. They reacted poorly to light in the optic atrophies, and unilaterally in the cases that

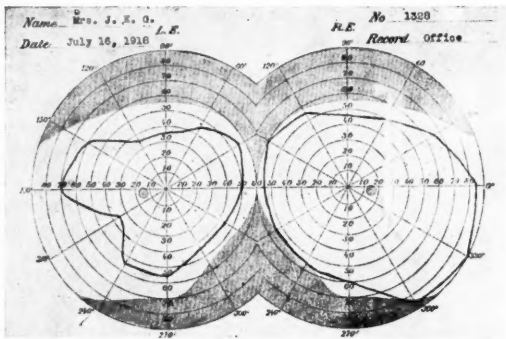


Fig. 257.—Perimeter fields, Case IX (July 16, 1918, by Dr. W. E. Shahan, St. Louis). Beginning contraction in the left upper temporal quadrant, slight in the left lower (right eye normal).

had other changes in the disk, such as choked disk or neuroretinitis. There was no fixation of the pupils in any of the cases, and no central blindness. The temporal side of the retina was reported as paler than usual in many cases, and in 1 case there were marked engorgement of the arteries, clubbing of the veins, and at one examination fresh hemorrhages scattered throughout the retina (during which time the patient was undergoing the terminal months of pregnancy). It is particularly interesting to note that in this case during the last months of pregnancy all the neighborhood and general intracranial pressure symptoms were so exaggerated as to cause the consulting oculist to give

a bad prognosis and urge intervention to relieve the intracranial pressure in order to prevent permanent blindness. These symptoms, however, cleared up without cranial operation after cesarean section at term. The changes in the perimeter field, retina, and disk receded to the state present at the onset of pregnancy and remained practically stationary, allowing the patient to continue her work (clerical) for five years after this bad prognosis was given, to the present time. This is a very

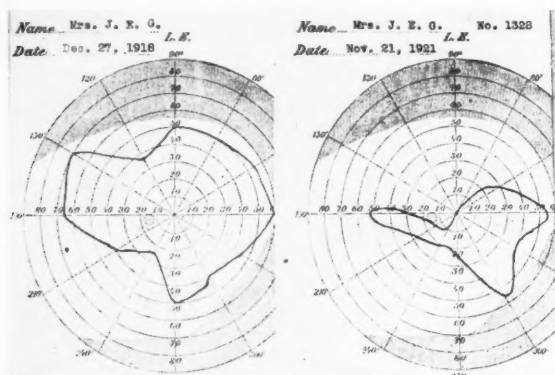


Fig. 258.—Perimeter fields, Case IX (December 27, 1918, and November 21, 1921, by Dr. W. E. Shahan), showing the left eye. The right eye is not shown because normal. In the left chart there is slightly more contraction of the left lower and upper temporal quadrants to form field than shown in Fig. 257. In the right chart there is more marked contraction to form of both temporal and nasal fields, affecting particularly from the 30° to the 180° meridian above and the 180° to the 300° meridian below.

good demonstration of the activation of an incipient or a non-progressive tumor by a pregnancy. It is a confirmation of the work of Erdheim and Stumme, who found that the hypophysis underwent a physiologic increase of one-third in size during pregnancy, and helps to explain the onset of some cases of hypersecretion producing acromegaly during pregnancy.

Other neighborhood symptoms, such as pressure upon other structures of the brain in the neighborhood of the pituitary gland, as the hippocampal gyrus or peduncles, were present in

only 2 of these cases. One of them had peculiar epileptic attacks which simulated uncinat epilepsy. There have been no complaints of interference with the olfactory or gustatory sense in these cases. None of them has progressed so far as to have nasopharyngeal signs or rhinorrhea. This is another sign that presents itself only as a terminal condition and should really not be considered as one of the signs of pituitary tumor, but rather as one of its late complications. In fact, if less significance were placed upon such conditions, an early diagnosis

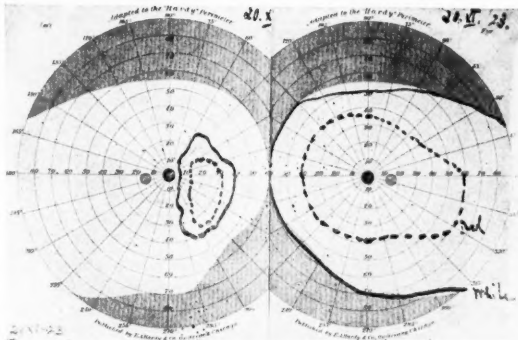


Fig. 259.—Perimeter fields, Case IX (November 20, 1923, by Dr. Carl Barck, St. Louis). Note the further contraction to both color and form in the left eye, which at this time has a complete hemianopsia, with a paracentral contraction of the nasal field to both form and color. During this time (July 16, 1918 to November 20, 1923) the right perimeter and the sella remained normal.

would more likely be made. These nasopharyngeal signs are comparable to the palpable tumor mass in the epigastric region as a diagnostic indication of malignancy of the stomach, or a demonstrable erosion of the sternum as a sign of aneurysm. In only one of our cases (No. 2) was there a sufficiently large tumor to produce a breaking through of the anterior wall of the sella turcica into the sphenoidal sinus. The anterior wall of the sphenoidal sinus, however, was not affected, and consequently no nasopharyngeal signs or rhinorrhea was present. Pressure upon the peduncles is frequently responsible for a disturbance

in gait, producing ataxia. This also was present in one of our cases (No. 1) as a terminal condition.

Another symptom which properly should be classed as a neighborhood pressure symptom in these cases is the *pituitary headache*. This headache is probably due to a direct pressure upon the capsule of the gland and the sellar structures from the enlarged pituitary, rather than to a general intracranial pressure. This is suspected on account of the intensity and severity of the headache, out of proportion to the size of the tumor. The patient frequently complains of pain directly in the eyes or eye

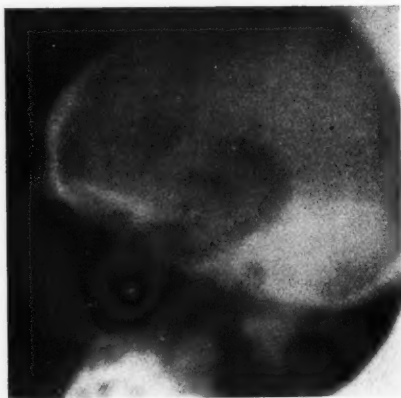


Fig. 260.—Sella, Case XI. Normal in size (the patient having a homonymous hemianopsia). Note the defect in the skull from a decompression operation.

having perimeter deviation. This pain in one case preceded the perimeter blindness for a short time. The pain frequently is localized at the root of the nose and just posterior to the eyes. In some cases it is described as a pain circling the base of the skull, extending posteriorly to the inferior portion of the occiput. It very rarely is located in the vertex of the head unless the tumor is large, in which case the cause of the headache is probably more an intracranial pressure than a localized pressure. It is considerably different from the ordinary attacks of migraine ophthalmique or classical migraine, which is so frequently as-

sociated with aneoplastic pituitary disorders. The headache in these cases is more likely to be unilateral, but varying from one side to the other during different attacks, and associated rather definitely (in a classical migraine) with scotomata and gastric symptoms, as nausea and vomiting. The diagnosis of pituitary headache, however, cannot be made upon the characteristic location, severity of pain, and associated ocular or gastric symptoms. There must be sufficient other evidence of pituitary disorder, such as osseous, genital, dermal, or pigimentary changes, accompanying these headaches to warrant such a diagnosis.

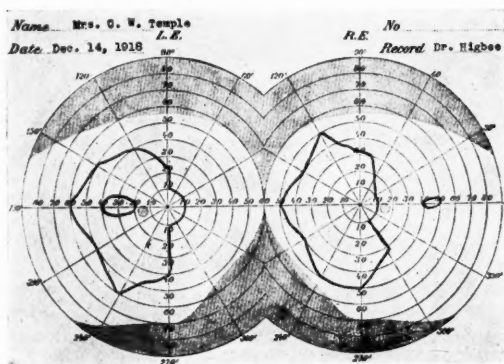


Fig. 261.—Perimeter fields, Case XII (December 14, 1918, by Dr. E. H. Higbee, St. Louis). Homonymous hemianopia. The fundus presented retinal hemorrhages and papilledema. The patient was in the terminal weeks of pregnancy.

The general intracranial pressure symptoms need no special review. They consist of the same signs as produced by any intracranial pressure process, such as vomiting, headache, choked disk, and photophobia. The vomiting has no relation to any other gastric disorder or symptoms and usually occurs quite suddenly, the patient having the typical projectile vomiting without nausea. No anorexia or localized symptoms about the stomach or abdomen are present. The photophobia is not one due to perimeter abnormality, but one associated with severe

headache, the patient usually feeling very much more comfortable if the eyes are closed and quiet in a dark room is obtained. It has usually been taught that every intracranial pressure lesion, whether due to tumor or other condition, must have headache as a cardinal and constant symptom. On reviewing the histories of these cases, it is noted that in 2 cases, which lasted six months to one and one-half years respectively, both of whom had unquestionable enlargement of the sella and perimeter signs, with general hormonal signs of pituitarism, *there was no*

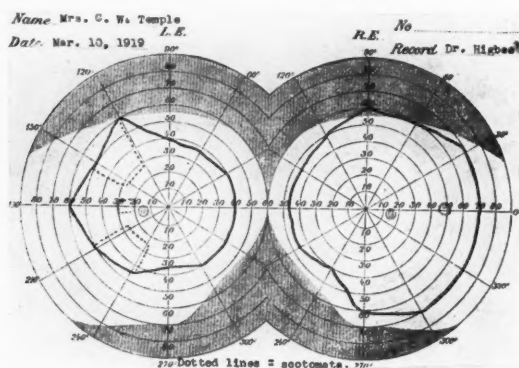


Fig. 262.—Perimeter fields, Case XII (March 10, 1919, by Dr. E. H. Higbee). Note the marked improvement in the form fields over Fig. 261, the right eye being normal, the left eye having only a moderate contraction of both temporal and nasal form fields, with partial scotomata. This improvement occurred following delivery.

*headache, nor had headache been a complaint during the course of the disease.* It is precarious, however, to make a diagnosis of any intracranial pressure process without headache. One should be reluctant to make such a diagnosis without having an overwhelming amount of objective evidence at hand.

In all of these cases, with the exception of one, there were outspoken general hormonal symptoms and signs of disorder of the pituitary gland. While it is true that there has been an attempt to overestimate the value of some of the neighborhood signs, we believe that, on the other hand, it is just as true *that*

*the general hormonal signs have been overlooked and given insufficient importance not only as absolute diagnostic signs of pituitarism, but also as signs which are localizing, i. e., specific for pituitary disorder. As will be seen from Table No. 1, these signs are objective changes in the osseous system, localized adiposity (such as the girdle adiposity characteristic particularly of pituitary disorder), polyuria (diabetes insipidus), complete and prolonged amenorrhea, and pigmentation (chloasma), each of which is specifically connected with pituitary disorder and not with other lesions of the central nervous system. In one case*

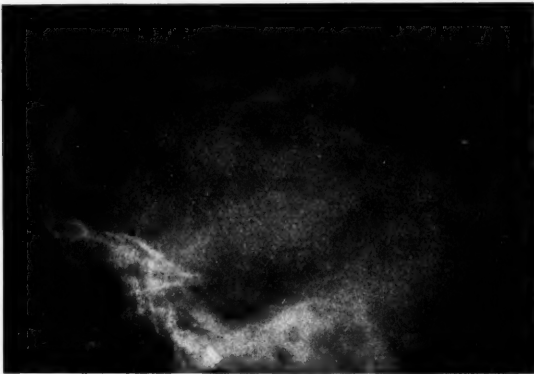


Fig. 263.—Sella, Case XIII. Note the enormous enlargement, measuring 13 x 23 mm. Erosion of the anterior and posterior clinoid processes.

(No. 11) the diagnosis of hypopituitarism had been made for three years previous to the development of homonymous hemianopsia. The early diagnosis of pituitarism was based upon the gradual decrease of the menses at thirty-two and final cessation at thirty-five. This was associated with the very classical chloasma pigmentation frequently found in cases of pituitarism. Of these 13 cases, 6 had polyuria, a sign which is being recognized as due to disordered pituitary function. Glycosuria was present in 3, in 1 of which it was very severe. In all cases it was considered a hypophyseal glycosuria on account of its peculiar dissociation from carbohydrate intake and hyper-

glycemia. In some of these cases the blood-sugar was very high, with a normal urine, and in other cases the blood-sugar was apparently normal, as in renal diabetes, with variable glycosuria. Classical pituitary adiposity was present in 4 cases, and in 1 case pituitary hibernation occurred.

The **course** and **progress** of these various tumors offer an unusual amount of interest, owing to the fact that they help to mold the prognosis and fix the indications for treatment, particularly that of surgical intervention. It is surprising to note that, of these 13 cases, with an average duration of five and one-half years, only 3 died. One had a very severe glycosuria and finally died in a state of coma, due to acidosis. This case had a positive specific infection and had been relieved for a considerable time by antiluetic therapy, which reduced the glycosuria and hyperglycemia and restored for a time the weight and general strength of the patient. During a later relapse, however, this same reaction to treatment did not occur. One died of pulmonary infarction from a chronic endocarditis, and one of general intracranial pressure symptoms. Of the other 10 cases, still living, the duration varied from one to fourteen years, and these have been under more or less constant observation. Of these, 2 have been operated upon and a number of others have been advised to have operation, on account of the positive signs of progress of the tumor growth, but have not accepted surgical treatment. A number have been advised against operation on account of the presence of definite symptomatology indicating absence of progression in size of the neoplasm. In fact, there was rather positive evidence of recession of the tumor, as proved by the subsidence of both neighborhood and general intracranial pressure symptoms. The general hormonal signs, when once established, rarely change, and do not serve as a guide relative to the return of function or continuance of growth of the hypophysis. One exception to this rule is the polyuria, which in a comparatively few cases disappears, indicating that there is a probable return of function of a lobe of the gland. Careful detailed analysis and interpretation of all the previous neighborhood and general intracranial pressure



symptoms bear upon the one point of establishing whether or not there is growth and progress of the tumor. In order to determine this progression it is necessary then not to accept the signs of one organ, such as the eye (perimeter fundus, etc.), but to take this as only a part of the evidence and add to it the size of the sella, as determined by serial comparative x-ray pictures, and the severity or progress of other intracranial pressure signs, such as headache, choked disk, photophobia, vomiting, etc. When all these signs are collectively considered, it usually is not difficult to determine whether the tumor is in an active, growing state or whether it has arrived at a stationary period, which may be followed later by recession. If all the signs of progression (deformity of the sella; ocular defects, as changes in the perimeter, disk, retina, pupil, and motor ocular nerves; and general intracranial pressure symptoms, as headache, vomiting, photophobia, etc.) are absent or in a state of recession, then at least further observation may be permitted. It should be provided, however, that a frequent check be taken upon all the neighborhood signs by serial ocular and sellar examinations, to make accurate determinations of the course of the neoplasm. On the other hand, if there is evidence of increasing neighborhood or intracranial pressure symptoms, it is dangerous to allow the growth to progress to such a state as to produce complete destruction of the optic nerve, as permanent blindness and other severe effects upon the neighborhood brain structures will certainly occur.

The **diagnosis** of hypophyseal neoplasm ordinarily is made with ease in the classical, rapidly growing tumor producing very characteristic signs in all three groups of the symptomatology. In those cases, however, in which there is no sellar deformity, the diagnosis becomes very much more difficult and requires a careful differentiation from other lesions in the neighborhood of the peduncles, occipital lobe, and cerebellar region, particularly if the general hormonal signs are not absolutely characteristic. The typical ocular changes, however, combined with the very classical general hormonal signs, even without sellar deformity, are frequently sufficient in themselves for such a

diagnosis. In the majority of these cases, if the opportunity for prolonged observation is afforded, deformity in the sella sooner or later is noted. As stated under the discussion on symptomatology, bilateral temporal hemianopsia is not always present and is obtained only at a certain stage of the course. For this reason, it should not be awaited for the diagnosis of pituitary neoplasm. Typical sellar deformity when present is often sufficient in itself for diagnosis. Another important diagnostic point in differentiating from other intracranial lesions is the long duration of the course of the pituitary struma. This is particularly true as compared with gliomas, which average a shorter duration. Differentiation from occipital tumors, owing to the fact that both may produce homonymous hemianopsia, rests to a large extent upon competent localizing ocular signs. Fixation of the pupil, central blindness, and changes in the macula lutea are very important. Other localizing signs referable to occipital tumor, such as localized pain, tenderness, pressure upon the cerebellum, etc., are of only insignificant aid. In all classical cases in which definite deformity of the sella turcica occurs, associated with the ocular signs mentioned above and intracranial pressure symptoms, the diagnosis is positive. Diffuse intracranial pressure symptoms, with general hormonal signs indicative of pituitary disorder, are hardly sufficient for a positive diagnosis, as a great many of the ordinary pituitary disorders not having a tumefaction as their etiologic cause have this combination.

**Prognosis.**—The prognosis in these cases as a rule is fairly good as to life, as has been noted from the duration of the cases of this series. It is comparatively unfavorable in regard to the establishment of a good capacity or freedom from more or less distressing symptoms. The severity of the case will depend upon the rapidity of growth, with resulting localized pressure effects, of the tumor. Consequently, the symptomatology referable to progression of the tumor, as derived from a careful interpretation of all symptoms bearing upon this point, is a most important means of determining the absolute prognosis in a given case at a certain time. A latent, inactive, or stationary

tumor which has produced only a limited amount of pressure and destruction of tissue in the neighborhood, offers a comparatively good prognosis as to prolongation of life, and really is no justification of radical surgical procedure. On the other hand, evidence of a rapidly growing tumor makes the prognosis dependent upon very active surgical intervention before the destruction of the optic tract, chiasm, or other important tissue in the neighborhood of the mass has taken place.

**Treatment.**—The indications for treatment in these cases depend upon the progression of the tumor at the time of observation. If there is evidence of a tumor which has become stationary, as occurs in some of these cases, particularly cyst of the hypophysis, there certainly is no indication for immediate surgical intervention. Probably nothing more could be accomplished by emptying a cyst or removing a tumor which is not producing more pressure upon the neighborhood tissue, than would occur if the patient were allowed to go along under observation without treatment. At least, a number of these cases that we have seen operated upon, which were considered practically stationary tumors, without progression, have had no relief from symptoms, such as ocular defects, retinal changes, and general hormonal signs, from which they suffered before operation. In these stationary tumors it must be considered that the general signs of intracranial pressure, such as headache, vomiting, etc., had disappeared entirely and the ocular and sellar changes, under repeated examination, had not changed for a considerable length of time. On the other hand, the treatment for rapidly growing tumor, which shows the signs of progress as demonstrated by only two groups of symptoms, the progressive ocular or sellar signs and evidence of increasing intracranial pressure, should be considered surgical. The patient with such a struma should not be allowed to go along until optic atrophy occurs and blindness becomes more or less complete and irretractible. Possibly one exception to this rule would be those cases giving an unquestionable specific history, with positive physical and laboratory reactions. These cases might be tried for a limited length of time on specific and x-ray treat-

TABLE II  
PITUITARY NEOPLASM

Total number of cases of pituitary tumor	13	
Total number of pituitary disorders	375	
Percentage of pituitary tumor	4 per cent.	
<b>Sella:</b>		
Larger than normal	9	
Normal size (one with erosion of posterior clinoid process)	4	
Erosions	10	
<b>Perimeter:</b>		
Bitemporal hemianopsia	2	(one changeable)
Homonymous hemianopsia	3	
Contracted field to form	4	(one left upper quadrant; three bilateral paracentral, one more marked in right, one more marked in left)
Unilateral hemianopsia	2	(one right, changeable; one left)
Normal	1	
Unobtainable	4	(one on account of blindness)
<b>Fundus:</b>		
Optic atrophy	4	(one right; one left; two bilateral, one relieved by treatment)
Choked disk	1	(bilateral)
Neuroretinitis	1	(bilateral)
Temporal pallor of retina	3	
Engorged vessels, retinal hemorrhage	1	(alive five years after bad prognosis)
Normal	4	
Unobtainable	3	
<b>Pupils and nerves (III, IV, VI):</b>		
Paresis of III and VI nerves	1	
Nerves negative	11	
Pupils equal	9	
Pupils unequal	3	
Disturbed light reaction	5	
Unobtainable	1	
Central blindness	0	
<b>General hormonal signs:</b>		
Osseous	4	
Polyuria	6	
Glycosuria	3	(one with hyperglycemia)
Adiposity	4	
Hibernation	1	

Menstrual .....	3	(one amenorrhea; one irregularity, with metrorrhagia and amenorrhea; one amenorrhea at thirty-five)
Impotency and loss of libido .....	2	
Muscle cramping .....	1	
Pigmentation (chloasma) .....	2	
Pituitrin test .....	3	negative
Adrenalin test .....	2	negative; 1 positive
Basal metabolism .....	5	(one +19 per cent.; one +35 per cent.; one +8 per cent.; one -1 per cent.; one -2 per cent.)
Progression:		
None .....	4	(one for four months; one for seven months; one for two years)
Regression:		
Rapid .....	1	
Rapid .....	4	
Gradual .....	4	(two benefited by x-ray)
Duration .....		one to fourteen years
Average .....	5½	years
Result:		
Death .....	3	(one of diabetic coma; one of pulmonary infarct; one of intracranial pressure coma)
Operation .....	2	(one decompression; one curettage of pituitary cyst)
High voltage x-ray .....	2	(productive of stationary course)
Stationary .....	5	
Regressive .....	1	
Progressive .....	4	

ment, on the basis of the possibility that the neoplasm is due to gumma of the hypophysis. If, however, this treatment is not effective in the course of six or eight weeks, it would be well to consider surgical intervention. In those cases in which there is evidence of rapid progression, who do not accept an operation, the only other means of treatment is x-ray and radium. In these cases radium is not very efficient on account of lack of deep penetration. High voltage x-ray treatment, focused upon the hypophysis through the temporal and frontal regions, beneath the hairline, has been effective in the hands of some men,

mostly of the foreign schools. We have recommended this as a second choice to a number of these rapidly growing pituitary tumors, two of which cases have taken it with apparently good results (Nos. 3 and 13).

With regard to the medical treatment, it has practically no field in these cases, except in a minor secondary rôle in those which have as a result of pituitary tumor a hyposecretion of one or both lobes. Substitution of these preparations to relieve the secondary hormonal signs, such as polyuria, obesity, amenorrhea, hibernation, pituitary headache, etc., may be given. It should always be borne in mind, however, that there is a very slight possibility of activating the pituitary tumor by giving these substances, and for this reason their effect should be observed very carefully and any signs or symptoms of hypersecretion should be cause for a discontinuance of this medication.

#### BIBLIOGRAPHY

1. Aschner: Pflüger's Archiv., 1912, 146, 1.
2. Bailey and Bremer: Ergebnisse der Physiol., 1922, vol. xx, p. 162.
3. Bauer, J.: Individual Constitution and the Endocrine Glands, read before St. Louis Med. Soc., November 27, 1923 (to be published in Endocrinology).
4. Biedl, A.: Physiologie und Pathologie der Hypophyse, Edition 1922.
5. Camus and Roussy: Compt. rend. Soc. de Biol., 1913, 75, 483, 628; 1914, 76, 121, 297, 344, 773, 877; 1920, 83, 764, 901, 1578; 1921, 85, 296.
6. Chanal: De la croissance au cours et dans la convalescence des maladies aiguës fébriles du jeune âge, de la fièvre typhoïde en particulier, Paris, 1907.
7. Cushing: The Pituitary Body and Its Disorders, Edition, 1910.
8. deSchweinitz: Jour. Amer. Med. Assoc., vol. 81, No. 21, November 24, 1923, p. 1768.
9. Erdheim and Stumme: Über die Schwangerschaftsveränderung der Hypophyse, Beitr. z. path. Anat. u. z. allg., Path., 1909, xlvii, 1-132.
10. Evans and Smith: Address before Association for Study of Int. Sec., San Francisco, June 24, 1923 (to be published in Endocrinology).
11. Kenneway and Mottram: Quart. Jour. Med., Oxford, 1918-19, xii, 225. Quoted by Rowntree in article on Diabetes Insipidus, Tice's practice of Medicine.
12. Lillie: Ocular Phenomena Produced by Intracranial Lesions Involving Optic Tracts Near the Chiasm, Jour. Amer. Med. Assoc., vol. 81, No. 21, November 24, 1923, p. 1765.
13. Messedaglia: Studi sull' acromegalia, Padova, 1908, 1-336; Estratto dal, vol. iv, A. de Giovanni, U. Hoepli, ed., Milano, 1908-09.

## CLINIC OF DR. RALPH A. KINSELLA

BARNES HOSPITAL

### HYPERTENSION AND NEPHRITIS

It is important to arrange our ideas concerning hypertension so that we may adopt a reasonable basis for our attitude toward this very important clinical condition. If we are inclined to regard hypertension as always a compensatory condition having a definite purpose, we must search for evidence to support such an idea in all our cases. We must cease to speak of essential hypertension in the sense of a disease *per se*, and we must realize that our therapeutics must be directed at the cause of hypertension in as far as this is possible. We must realize and we must make our patients realize that high blood-pressure in itself is not a target for therapeutics.

In approaching this subject, it occurred to me that a good classification of disease of the kidney is desirable, and for this purpose one of your class, Mr. Walter B. Wolfe, has translated and will present in abstract the work of Volhard and Fahr.

#### DIE BRIGHTSCHE NIERENKRANKHEIT

In making this abstract of the work of Volhard and Fahr it is possible only to touch on the salient features of this very complete and carefully written treatise.

Although in the beginning Bright's disease was a term applied only to diseases of the kidney associated with albuminuria and dropsy, today it is applied in a far broader sense and includes a variety of degenerative, inflammatory, and arteriosclerotic processes which are now clinically known as nephritis. The researches of Volhard and Fahr attempted to align the clinical, the pathologic, and laboratory findings in these diseases.

According to this book, the degenerative nephropathies are designated as nephrosis, the inflammatory as nephritis, and the arteriosclerotic as sclerosis.

#### CLASSIFICATION OF NEPHROPATHIES

A. Nephrosis: Genuine and of known etiology, with and without amyloid degeneration.

1. Acute. 2, Chronic. 3, Terminal: Nephrotic contracted kidney without increased blood-pressure.

B. Nephritides.

1. Diffuse glomerulonephritis with compensatory increased blood-pressure in three stages.

- |  |   |   |
|--|---|---|
| <ul style="list-style-type: none"> <li>(a) Acute</li> <li>(b) Chronic with insufficiency</li> <li>(c) Terminal with insufficiency</li> </ul> | } | <p>All three stages may run a course:</p> <ul style="list-style-type: none"> <li>(a) Without edema.</li> <li>(b) With edema and marked and diffuse degeneration of the epithelium.</li> </ul> |
|--|---|---|

2. Focal nephritis, without increased blood-pressure.

- (a) Focal glomerulonephritis, acute and chronic, Streptococcus viridans, Endocarditis.
- (b) Septic interstitial nephritis.
- (c) Embolic focal nephritis.

3. Sclerosis.

- 1. Benign hypertension—pure sclerosis of kidney vessels.
- 2. Malignant hypertension—the combination form, so-called genuine contracted kidney or sclerosis plus nephritis.

#### NEPHROSIS

This term includes all degenerative lesions, cloudy swelling, granular and fatty degeneration, and necrosis of the kidney in which there is definitely no inflammation or the inflammation is undemonstrable.

The clinical picture includes what was known formerly as



chronic parenchymatous nephritis without increased blood-pressure, and is represented by kidneys showing granular degeneration and fatty degeneration of the epithelia of the tubules without inflammatory change in the glomeruli. They are much less frequent than the other nephropathies. The etiology is usually bacterial toxins, pregnancy, and cachexia; also after poisoning with the heavy metals, particularly mercury, arsenic, bichromate, etc.

The chief symptom is edema; kidney function is usually unimpaired, diagnosis may be made by the absence of increased blood-pressure, the presence of edema, urinary findings, and good kidney function. The prognosis, so far as the death from the kidney condition goes is good, but it is entirely dependent upon the underlying cause.

One important variation is the bichlorid kidney. Here there is no marked edema, there is frequently anuria, function is poor, non-protein nitrogen high, low phenolsulphonephthalein, and signs of uremia are present.

#### NEPHRITIS

No etiologic basis of classification is permitted with present knowledge. Volhard and Fahr say:

1. The pathogenic cause of every nephritis is almost without exception a bacterial infection.

2. Increased blood-pressure is a characteristic feature of diffuse glomerulonephritis. Its presence in an acute kidney disease is diagnostic. Urine is usually decreased, contains blood.

Glomerulonephritis is separated functionally into the two following stages:

- A. Early stage: Blood-pressure is increased and there is usually some cardiac hypertrophy. Edema is not an essential sign. Uremia never occurs. Urine corresponds to fluid intake. Albumin present, but variable, usually small. Eye-grounds often show changes. There is no marked impairment of kidney function at this stage. Nutrition is poor and recurring edema may be a feature.

- B. Late stage: Usually occurs before fourth decade. Symp-

toms absent until just before the end. No recidives or exacerbations. Constantly maintained high blood-pressure, with marked hypertrophy of heart, with signs of cardiac decompensation. Blood shows marked secondary anemia. There is polyuria and albuminuria. Eye-grounds show constant papillitis and neuroretinitis. The chief characteristic is impaired function. Day and night polyuria, fixed specific gravity of 1.012, night lower. High non-protein nitrogen, creatinin, and low phenolsulphophthalein. There is true uremia, contracted pupil, digestive disturbance, hyperirritability, dyspnea and fall of temperature; apathy, stupor, coma, and death follow.

Further investigation showed that inflammatory processes may occur in the absence of increased blood-pressure. These cases included a group of hemorrhagic focal nephritides such as embolic focal nephritis described by Lohlin, which occur chiefly in *Streptococcus viridans* sepsis, and in the acute interstitial focal nephritis (of Councilman) which occurs after scarlet fever and septic processes like scarlet fever and streptococcus angina.

#### THE SCLEROSIS

The conception that chronic interstitial nephritis was not an inflammatory disease, but was due to arteriosclerotic processes in the small and smallest vessels of the kidney was first formulated by the pathologists Jores, Fahr and Janeway, and in 1914 Volhard and Fahr published their observation. The designated as benign hypertension, that clinical condition in which there could be found no evidence of impaired kidney function, in which the kidney macroscopically showed contraction or was uncontracted. From this clinical entity they differentiated malignant hypertension, the so-called combination form in which there was superimposed nephritis of inflammatory origin, on an original arteriosclerotic process, a picture which showed very much impaired kidney function, and was represented pathologically by kidneys showing inflammatory or degenerative changes plus arteriosclerosis.

**BENIGN HYPERTENSION**

1. Occurs after the fortieth year and is quite common.
2. Runs its course as a cardiovascular disease. The first symptom may be that of relative myocardial insufficiency, which retrogresses to complete degeneration.
3. The general condition is good, the patient appearing healthy, being usually of a plethoric habitus, active, ruddy complexioned, stocky in build.
4. There is high blood-pressure, with transitory rises.
5. The heart is markedly hypertrophied, showing left ventricular hypertrophy.
6. The relative infrequency of anemia is an important diagnostic differentiation from the glomerulonephritides and the combination form.
7. The urine is usually negative, there may be nycturia, and a moderate night polyuria.
8. Eye-ground changes are always those of arteriosclerosis, never of chronic nephritis.
9. Kidney function is unimpaired.

**MALIGNANT HYPERTENSION**

1. From forty to fifty years of age.
2. Condition rapidly declines and patient becomes cachectic.
3. Cardiovascular symptoms more severe than in the benign type.
4. The blood-pressure is consistently high and is constantly maintained.
5. Cardiac hypertrophy is very marked, and the largest hearts are found.
6. Edema is always of cardiac origin.
7. The blood shows more severe secondary anemia in contrast to benign.
8. There is always nycturia and day and night polyuria, low specific gravity.
9. Impairment of function is the chief feature of this type. These cases end with true uremia, as in the end stage of

chronic glomerulonephritis, if vascular accident or intercurrent infection has not intervened.

#### DISCUSSION

This classification is based entirely on clinical and pathologic findings and represents painstaking work.

I think that whatever the changes that may be made in this classification in the future, at the present time it offers the best basis for considering cases of kidney diseases and cases of hypertension. One feature in this classification is the failure to give any importance to syphilis in the third group, where cardiovascular diseases is a feature. Of great importance in this classification is the factor of increased blood-pressure. This is used to separate the first and second group and to subdivide the second group. It is extremely important to note that increase in blood-pressure is associated with glomerular and other blood-vessel disease. It is important to realize that there are mixed forms.

There are forms of nephrosis in which secondary chronic inflammation may produce a picture of chronic nephritis if such chronic inflammatory changes affect large numbers of glomeruli.

There are clinical cases of albuminuria with occasional edema with low blood-pressure which seem originally to have been glomerulonephritis of a less diffuse character than the usual form. Little attention is paid in this classification to those cases of nephritis associated with and apparently caused by infection of the urinary tract with retrogressive involvement. Of greatest importance perhaps to practitioners is the group of sclerosis because this condition is so frequently encountered.

Now we wish today particularly to establish the relation of hypertension to nephritis as we have in other cases that we have presented. We are especially concerned with defining types. In these cases of edema and cardiac dilatation the use of digitalis is sometimes strikingly beneficial. Not only does the edema disappear and the weight fall, but the accompanying increase in urinary output is coincident with an increase in blood-pressure. We have seen this combination several times.

**Case I.**—As an example of the benign hypertension, here is the record of a colored physician who is thirty-eight and entered the hospital because he knew his blood-pressure was high. He had no nocturia, his kidney function was good, his phenol-sulphonephthalein excretion 55 per cent. in two hours; non-protein nitrogen 32 mgm.; uric acid 3.9; normal blood-sugar. No symptoms of nephritis or hypertension. Remember that he did not have nocturia. Blood-pressure varied from 170/120 to 184/130. A feature of his blood-pressure was its tendency to be easily reduced and elevated. His capacity to concentrate as indicated by the specific gravity of his urine was good.

The point of interest is this, that without the work of Volhard and Fahr, which supplies an insight into the pathology of the kidney in just such a case without demonstrable kidney dysfunction, without symptoms, such a case might have been called essential hypertension; but with a knowledge of the pathology of the kidney, we are able to remove even this type of case from the category of essential hypertension and call it distinctly secondary hypertension on the basis of pre- and post-capillary fibrosis. What will be the fate of such a case in later life? Will this man who is now thirty-eight become ill with kidney disease or will he become ill with symptoms of vascular disease, and vascular accident, or with cardiac disease, and circulatory failure? He already has some enlargement of the aortic arch and his electrocardiogram shows left ventricular preponderance.

He has had a severe infection of the tonsils and is thought to have chronic infection of the ethmoid sinuses. You are aware of the importance of eliminating such infected foci. Frequently higher pressures are maintained in the presence of these infections than after their removal. This may be due to the infection of the already damaged kidney by such foci. If the kidney changes in this case become quiescent it is conceivable that a long life may follow. This is a patient who needs careful advice as to his general hygiene and habits. He needs no drugs. If his blood-pressure shows a tendency to rise, this may be accepted as a sign of increasing damage to his renal

capillaries. Infections anywhere in his body will contribute to this damage. He must keep his energy output within reasonable limits and sleep will be the most important feature in dealing with this phase. Diet should be sensible.

**Case II.**—Here is a case of a woman forty-nine years of age who lives a very quiet life, who has many symptoms. Blood-pressure varies from 215/115 down to 170/95. She complains of symptoms of angina pectoris. She has nocturia pronounced. She has occasional headache, and she has numbness occasionally in the left arm and left foot. No doubt she has had hypertension a great many years. She has at present signs of renal insufficiency. Phenolsulphonephthalein is 35 per cent. in two hours, blood chemistry normal. Here is an illustration of a case of hypertension which has very likely gone from benign hypertension into a more malignant stage. There is extensive left ventricular hypertrophy, and enlargement of the aortic arch with a loud systolic murmur in the second right interspace. Wassermann is negative.

In this stage with such a degree of involvement of the cardiovascular system, we can predict that the outcome will undoubtedly be cardiovascular failure. Perhaps it will be sudden failure, with angina pectoris, perhaps the numbness on the left arm and left foot are warnings of apoplexy later on. This condition is extremely serious. She is just as much a hospital case as a person with severe diabetes or extensive tuberculosis. Only a considerable period of rest in bed will indicate the degree of reclamation possible. The use of sodium nitrite and sodium bromid are urgently indicated.

Next patient presented by Student.

**Case III.**—**STUDENT:** This patient was brought to the hospital in an ambulance, with the chief complaint of swelling in legs, enlargement of abdomen, and shortness of breath, and a headache which is not continuous. Family history seems to be negative. Past history: Patient claims to have always been well. Claims not to have had the usual childhood diseases,

malaria, typhoid, or any other disease, but about three or four years before present illness started, which was November, 1922, had a rather indefinite history of severe headaches. Also coughs and produces a sputum which she said was of greenish material. Present illness began November, 1922 with shortness of breath, some swelling of extremities, and that seems to be about all. This gradually increased, becoming worse the last three months. Patient brought in in an ambulance in a condition somewhat worse than she is now. Very short of breath; edema was great in abdomen and extremities. Wassermann negative. Red cells over four millian, hemoglobin 70 per cent. Urine at start had small amount of albumin, many W. B. C., but rarely a cast. Total amount of urine less than 500 c.c. excreted at night, about as much as during the day. Eye-grounds are normal. They do not show sclerotic arteries. Concerning the heart (x-ray picture being passed), the angles between the auricles and ventricles are marked, which help to distinguish from pericardial effusion. Rate was regular. Second sound increased over all areas. No murmurs heard. Heart enlarged to left and to right.

QUESTION: Has this patient fluid in her pericardium, or is her enlargement entirely due to dilatation? What are the best diagnostic points for determining the presence or absence of fluid in the pericardium?

ANSWER: Heart sounds are decreased in cases of pericardial effusion and are heard nearer the sternum than in dilatation. Here the heart sounds are heard at the outer limit of dulness. From the standpoint of the fluoroscopic examination, the mobility of the heart border if the pericardium is distended with fluid is very much lessened. In this case the mobility of the outline of the shadow is very marked, and is complete with each heart beat.

In spite of the circulatory failure, the blood-pressure is 250/160. There are signs of renal failure. The dye excretion is only 15 per cent. in two hours, and the blood non-protein nitrogen is 48 mgm.

DR. KINSELLA: Although this patient was free from symp-



toms before November, 1922, it is very likely that she had hypertension long before. Her statement concerning headaches may indicate this. What do you think is uppermost in this case, kidney failure or cardiovascular failure?

STUDENT: Kidney failure primarily, circulatory failure secondarily. Dye excretion of 15 per cent. if continuous is a serious impairment and non-protein nitrogen of 48 is a definitely increased retention. The low dye excretion may be affected by the passive congestion. The outstanding feature here is cardiovascular failure.

DR. KINSELLA: This is a case of malignant hypertension which belongs to the final subdivision of the third class of nephritis. There are no signs which would point to an impending apoplexy. There is no numbness in hands or feet, or any pains on one side of the head. Here is a case in which kidney disease and cardiovascular damage are progressing hand in hand. What is apt to be the termination of a person with such cardiovascular disease and kidney failure?

Probably coma in which there is no sign of vascular accidents. A case that has progressed to a severe stage and shows no signs suggestive of weakness of the arteries would ordinarily end in uremia of the active type, not the quiet comatose case of uremia, but the case of uremia with convulsions.

We have gotten some insight into the fate of people with hypertension and nephritis. I think from the evidence we have considered, it is perfectly clear that any case of hypertension is secondary most probably to nephritis. Other causes for the production of continued hypertension are not established. You are all familiar with the various physiologic influences which raise blood-pressure in normals, but none of these various causes, such as diet, mode of living, excitement, has been established as a producer of continuous hypertension or as a producer of nephritis. As a further illustration that hypertension is a compensatory reaction and has a purpose, we have a case of a young girl twenty years of age, a student, who entered the hospital with a pressure of about 180/100, who had occasional polyuria. She knew that she had kidney trouble because



her urine had previously been examined and albumin had been found. She is occasionally easily fatigued, but has no headaches. She had chronic tonsillitis, and following tonsillectomy a severe hemorrhage occurred in which the systolic pressure fell to 100 and diastolic about 40. Now, then, it is perfectly plain to all of you that many normal young adults enjoy perfect renal function at a systolic pressure of 100. Furthermore, her pulse pressure was of some significance. The early work of Erlanger and Hooker shows that urinary secretion follows in direct proportion to the degree of pulse pressure, that is, the greater the pulse pressure, the more urine secreted. What happened to this person when her blood-pressure fell from 180 to 100? She immediately went to anuria with increasing non-protein nitrogen up to 115 from a previously normal level. Mental signs appeared and muscle irritability was apparent. Every effort was made to increase blood-pressure. We are not sure the favorable outcome was due to our efforts. Transfusions of glucose and massive dosage with digitalis were employed. Urination was resumed after three days, when the systolic pressure rose to 140. In other words, this person evidently had a hypertension for the purpose of secreting urine. Hypertension had a definite purpose and with a normal blood-pressure that the patient was unable to perform normally the secretion of urine. This suggests an optimum pressure not only for normal kidneys but also pathologic kidneys, and it is possible that there is a high pressure at which urine secretion is difficult, and this high point of pressure is particularly applicable in people with so-called malignant hypertension.

In this connection, the symptom of nocturia is very interesting as suggesting an adjustment between this pressure and urine secretion. Nocturia is a common symptom in hypertension, particularly in people with marked high blood-pressure of 180 to 200. We know that blood-pressure falls during sleep. It's quite likely that during sleep in these cases the kidney is active at a pressure which is much more agreeable to production of urine than during the daytime. Thus one of our recent patients had a pressure of 260 in the daytime and 215 during

sleep and pronounced nocturia. One of the patients whose record I just read had a daytime pressure of 215 and a nighttime pressure of 170, and that person had a marked nocturia. This offers a basis for the symptom of nocturia. As to the modern physiologic work on urinary secretion, I think that one thing is established in all the work, and that is, that there is a definite relationship between blood-pressure and kidney function. Mr. G. reviewed that work for you several weeks ago and pointed out that the work of Erlanger and Hooker, of Richards, and of Dreyer and Verney established one point while they may disagree on others, and this is, that urine secretion varies with blood-pressure.

The treatment of all these conditions, you can readily see, must be considered as the treatment of the underlying condition, and unfortunately it is usually extremely difficult to affect the underlying nephritis. If excessive use of salt or excessive use of water are contraindicated, it is very likely that these substances do not affect blood-pressure as much as they do damage to an already embarrassed kidney. However, many of you have observed in doing the so-called concentration diuresis test that the drinking of 2 liters of water produced marked discomfort and nausea in patients with excessive hypertension. Daily periods of rest are important, such as having a patient rest for one hour in the early afternoon. One thing is important to remember, that is, hypertension by itself is not the thing to be treated. Patients should understand that they are very much better off with a moderately raised blood-pressure than they would be with a low pressure. Falling blood-pressure is a clinical feature which has been repeatedly discussed as accompanying clinical failure in people who have previously had high pressure. If our patients can understand this "functional" character of hypertension they will be relieved of much of the worry which characterizes such patients and which itself is conducive to still higher levels of pressure.

## CLINIC OF DR. McKIM MARRIOTT

ST. LOUIS CHILDREN'S HOSPITAL

---

### NEPHRITIS IN CHILDREN

1. Acute Parenchymatous Nephritis (Nephrosis). Clinical Picture. Etiology. Relation to Infection. Nature of Condition. Treatment.

2. Acute Hemorrhagic Nephritis. Nature of Condition. Treatment.

**Case I.**—The first patient presented today is a girl four years of age. She comes from a family in which there seems to be a tendency to chronic nose and throat infection. The father has had a chronic "catarrh" and 2 other children are frail and have suffered from nose and throat infections and 1 has cardiac disease. The significance of this family history will be apparent later.

The patient has had frequent head colds each winter which have persisted for weeks. Aside from this she has been fairly healthy until the time of the present illness, which began four months ago, following exposure to cold and dampness. She had a nose cold at the time and this became worse. Shortly afterward the mother noticed a swelling of the lower extremities. Later the eyelids became puffy. The urine diminished greatly in volume and was dark colored. There was slight fever at this time.

The patient was seen by the family physician, who examined the urine and made the diagnosis of "kidney trouble," and the diet was limited to milk and cereals. The intake of fluid also was limited. The patient's edema diminished slightly on this treatment, but her general condition became worse. The patient was taken to another physician, who prescribed a salt-free diet with a minimum amount of milk and some cereal and green

vegetables. Meat and eggs were entirely eliminated from the diet and the fluid intake was restricted. This caused a temporary decrease in the edema, but the child became weak and anemic. She returned home and was put on a more liberal diet. The edema became more marked and continued up to the time of admission to the Children's Hospital. This was four months after the onset of her first symptoms. The edema had never completely disappeared during this time interval.

On admission she presented the typical picture of "the large white patient with the large white kidney." The skin was white and pasty. A generalized edema was present and the eyes were puffy and practically closed. The abdomen was distended with free fluid. There was a moderate amount of mucopurulent nasal discharge, and this was found on examination to come from the right superior meatus and the left middle meatus. The tonsils were large and cryptic. Cervical glands of the anterior and posterior chains were enlarged on both sides of the neck. Examination of the chest revealed nothing abnormal. Abdomen negative except for fluid as mentioned. Nothing else unusual in physical examination.

Laboratory findings: Wassermann negative. Von Pirquet negative. Red blood-cell count 4,000,000. White blood-cell count 10,000; 68 per cent. polymorphonuclears. Hemoglobin 60 per cent. Non-protein nitrogen in blood 27 mg. Blood-pressure 105/80.

Urine, twenty-four-hour specimen, volume 150 c.c. Specific gravity 1040. Acid in reaction. Very large amount of albumin. Microscopically numerous hyaline casts and occasional white blood-cell.

Phthalein functional test first hour 45 per cent., second hour 15 per cent., total 60 per cent.

The diagnosis of subacute parenchymatous nephritis is obvious.

Before undertaking the treatment it is necessary to have an understanding of the nature of the condition. Although we have made the diagnosis of "nephritis," it is well to realize that the condition is not really one of inflammation of the kidney as

the term "nephritis" would imply. In cases of this type there occurs swelling and degeneration of the cells lining the renal tubules. These cells are cast off and appear in the urine as "casts." Cells regenerate to take the place of those destroyed. The permeability of the kidney for the proteins of the blood is increased so that "albumin" passes into the urine. There is no involvement of the glomeruli, no true inflammatory reaction, and no fibrous tissue formation. Despite degeneration of the tubule cells the function of the kidney is good in most respects. There is no retention of urea or non-protein nitrogen. The phthalein test shows good function. The changes in the kidney are not permanent and complete repair is possible.

In view of the fact that there is not a true inflammatory reaction present the term "nephrosis" has been suggested as a more suitable one than "nephritis." The condition is also sometimes known as "tubular nephritis."

The question now arises as to the explanation of edema. At first thought one would say that the edema occurs because the kidney fails to excrete fluids or salts, but this is not a correct explanation. It has been observed that no edema occurs when both kidneys are removed. Furthermore, when the cells of the tubules degenerate as the result of certain poisons edema is not observed. We must, therefore, look for another explanation. From recent work we are led to conclude that the edema is the result of a change in the permeability of vessels and cells throughout the body, *i. e.*, fluids and salts pass through vessel walls into cells and serous cavities in an abnormal way. In this way fluid is held back in the body so that the kidney is unable to excrete it even if kidney function were in itself entirely normal.

Dr. S. W. Clausen, working in the laboratories of this hospital, has found present in the blood of all patients of the type here presented a substance capable of changing the surface tension of the blood and permeability of cells. This substance is excreted in the urine. The nature of this substance will not be discussed further at this point except to say that it is evidently produced in the body as the result of infection. From

the experimental work done here it appears likely that this same substance is responsible for the changes occurring in the kidney.

According to the ideas just outlined the patient is suffering from a systemic condition in which the kidney, as well as other portions of the body, are involved, and this condition is the result of infection.

The next step is to find and remove the infection, if possible. We have found in the last 20 cases of nephritis of this type coming to the hospital that there was an infection in the nasal accessory sinuses, and we have further found that the infecting organism was a staphylococcus in all of the cases examined. It is not to be concluded from this that staphylococcus infection of the nasal sinuses is the only cause of nephrosis. We do believe, however, that practically every case is the result of an infection and that the most common variety of infection is that just mentioned.

In this patient it was evident that abnormal conditions existed in the nose and throat. The first step was the removal of the tonsils and adenoids. Local treatment consisting of irrigation and the application of mercurochrome was carried out by Dr. M. F. Arbuckle, with the result that free drainage of the sinuses was established. One antrum was irrigated and pus obtained. The organism found was a *Staphylococcus aureus*.

Coincident with the clearing up of this infection the child's temperature, which had been ranging from 100° to 101° F., fell to normal and simultaneously there was a rapid and complete disappearance of the edema. There was a drop in weight from 44 to 28 pounds in the course of four days. This drop in weight of 16 pounds was due to loss of fluid. The volume of urine greatly increased during this time, and at the end of a week the urine was entirely free from albumin and casts and has remained so until the present time. The child's weight has subsequently increased slowly, but you will notice on examining her that there is no evidence at all of edema.

Local treatment of the nose and throat is being continued, and this is necessary because we know from observation of other patients of the same type that all of the symptoms of

nephritis are likely to recur should reinfection of the nasal accessory sinuses take place.

You will notice that we have said nothing as yet regarding the diet of this patient, and that is because the diet is relatively unimportant in the treatment of nephritis of this variety. Restriction of salts and of fluids will cause a diminution of the edema, but the effect will be only palliative. There is no need for restricting protein, as there is no nitrogen retention, as shown by the fact that the N. P. N. of the blood was just within normal limits. There is, indeed, a need for considerable protein in order to make up for the loss of albumin in the urine. Furthermore, protein often exerts a favorable rather than an unfavorable influence on the edema. This patient's diet was a liberal one, fluids were not restricted, and the same diet was maintained throughout her stay in the hospital. The disappearance of the edema was in no way dependent upon changes in the diet, but was the result of removal of the source of infection.

The principal lesson to be learned from this patient is that in the case of a child suffering from edema and albuminuria the first procedure is to search for and eliminate the source of infection, wherever that infection may be found. It is important to realize that children and even very young children may have definite involvement of the nasal accessory sinuses. It is, furthermore, of interest that a tendency to sinus infection seems to be hereditary. This child, as well as others whom we have studied, comes from a family in which there is a marked tendency to nose and throat infection. Such infections do not by any means necessarily lead to nephritis. There may be simply a low-grade continued fever and other organs of the body other than the kidneys may be involved. The combination of frequent and prolonged head colds with slight fever and especially the enlargement of posterior cervical chain of lymphatic glands should always lead one to search for suppuration in the nasal accessory sinuses.

**Case II.**—In contrast to the preceding patient I wish to show one suffering from an entirely different form of nephritis, due also to infection, but infection of a different type.



This patient is six years of age. He has had several attacks of acute tonsillitis, but has been well otherwise. Two weeks ago he had an acute attack of sore throat which lasted for about three days. Following this the mother noticed that the urine was cloudy, reddish brown, and apparently contained blood. There was no fever except during the acute attack of tonsillitis. No edema was noticed.

The boy does not appear acutely ill, and the general physical examination is essentially negative except for the fact that the tonsils are scarred, embedded, and slightly inflamed. The blood-pressure is 140/100.

The laboratory findings are of especial interest. The non-protein nitrogen of the blood is 80 mgm. per 100 c.c. The total volume of the twenty-four-hour specimen of urine is 1200 c.c.; specific gravity 1020. A moderate amount of albumin is present and microscopically there are large numbers of red blood-cells and a few white blood-cells. The phthalein test showed 20 per cent. excretion in the first hour and 5 per cent. in the second.

We have here then a very different clinical picture than that presented by the last patient. This is the type of nephritis ordinarily known as "hemorrhagic" or "acute glomerular" nephritis. In this condition there is involvement of the renal glomeruli rather than of the tubules. A definite inflammatory reaction may be present so that ultimately fibrosis and scarring occurs. The damage in most cases is slight, and may be recovered from entirely, but at times more permanent damage may occur. There is considerable alteration in kidney function during the acute stage. There is retention of urea and non-protein nitrogen. The phthalein excretion is diminished. Chlorids may be retained in certain instances.

The condition here is also a general one, so that in marked cases there are changes in the capillaries throughout the body, and this doubtless leads to the increased blood-pressure observed in cases of this type.

The cause of hemorrhagic nephritis is also usually infection, but the infecting organism is generally a streptococcus instead of a staphylococcus. The common focus of the infection



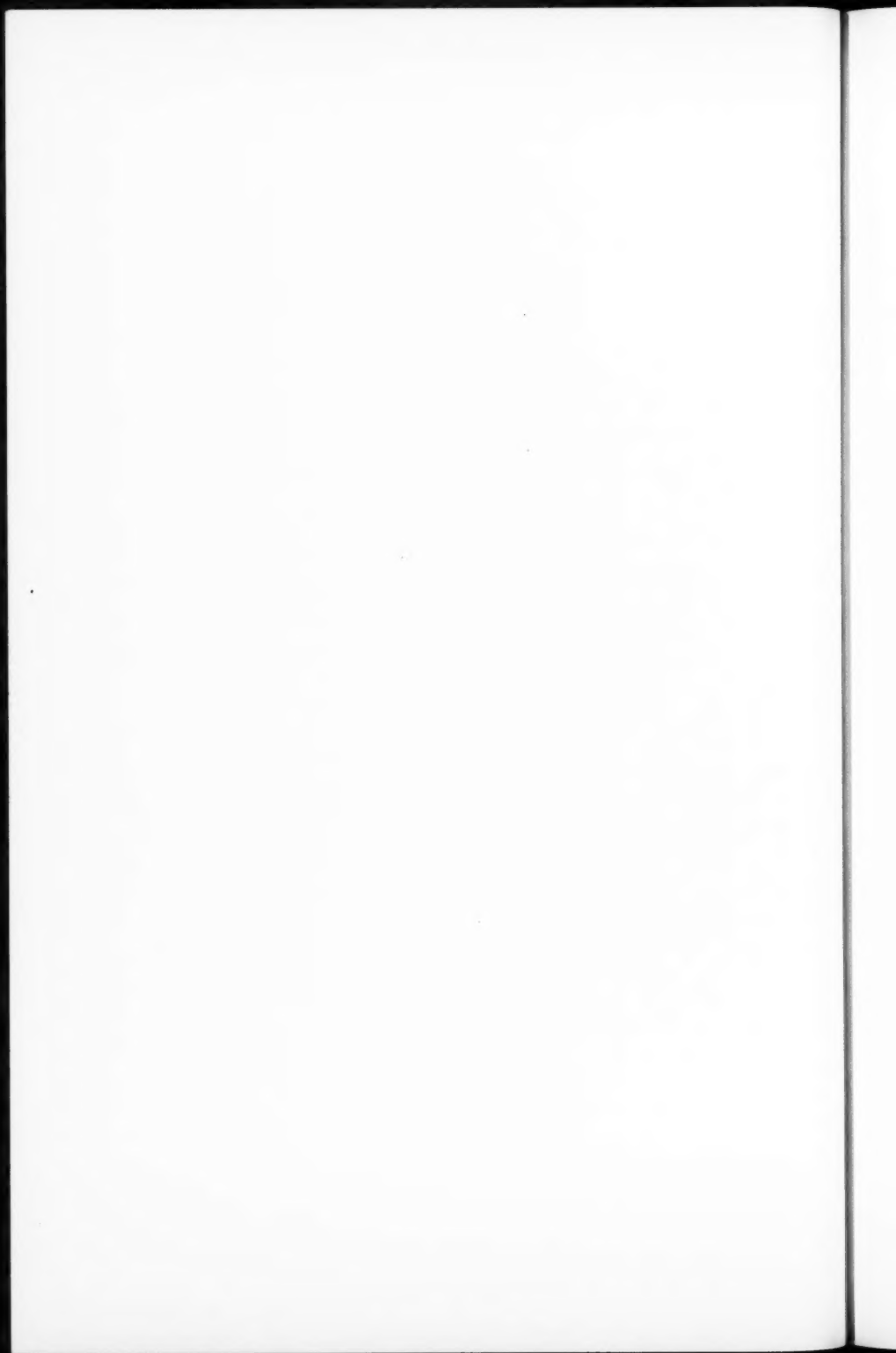
is in the tonsils, although streptococcus infection elsewhere may lead to the condition. When the infection is removed the evidences of nephritis slowly disappear in mild cases, but where the infection has been of longer standing permanent damage to the kidney with fibrosis and permanent damage to the systemic capillaries may occur, so that the end-result may be chronic nephritis with high blood-pressure.

In the treatment of a case of this type removal of the source of infection is the first essential. Such a patient should have the tonsils and adenoids removed if infected, or foci elsewhere should be cleared up.

The diet is important in cases of nephritis of this type. Proteins must be definitely limited on account of the tendency to nitrogen retention. The administration of protein not only tends to increase the non-protein nitrogen of the blood but also to irritate the kidney so as to lead to an increase in hematuria. Milk protein is less likely to do this than other forms of protein, and therefore milk should form the basis of the diet. Cereals may be added to advantage, but meat must be restricted for a considerable time. A large intake of fluid is an advantage.

As there is, in some instances, a retention of chlorids by the kidney the diet should have a very low salt content. When chlorids are administered freely to patients with this type of nephritis edema is likely to occur. This is rarely as marked as in the case of the tubular nephritis or "nephrosis." The edema is the result of salt retention by the kidney and not the result of retention of chlorids and salts by the tissues as in the other type of nephritis.

The 2 patients you have seen illustrate the two most frequent types of nephritis occurring in childhood. The one point they have in common is that each are due to infection. The results of the infection are, however, entirely different and the methods of treatment adopted are, in general, almost opposite. It is essential to recognize these facts.



## CLINIC OF DR. BORDEN S. VEEDER

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE<sup>1</sup>

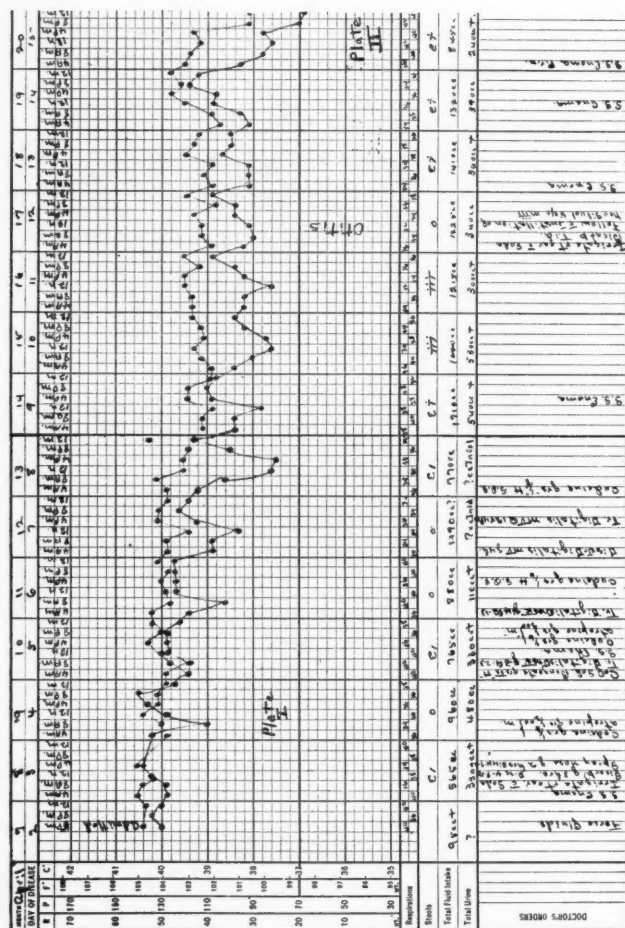
### A DISCUSSION OF SOME OF THE DIAGNOSTIC PROBLEMS OF LOBAR PNEUMONIA IN CHILDREN

IN contrast to this case of lobar pneumonia which is quite ordinary and typical in its course and manifestations, I wish to discuss with you a case which was in the hospital a short time ago which was quite unusual, as it brought up most of the important variations from the norm which pneumonia shows in childhood and raised a number of important diagnostic questions.

The patient was a boy five years of age whose clinical chart (Fig. 264) I will pass around. For about ten days before the development of the pneumonia he had had a mild upper respiratory infection with a catarrhal otitis media which cleared up without the necessity of a paracentesis. On the evening of the day previous to the day of admission to the hospital he developed a high fever which continued throughout the night. When I reached his home to see him the following morning I found him just coming out of a severe general convulsion which had lasted some fifteen to twenty minutes. The physical examination was negative. His temperature remained high all day and the child was quite toxic. From the toxicity, high fever, and negative findings in the throat, ear, and urine a tentative diagnosis of pneumonia was made. His condition remained unchanged until the next day (the day of admission to the hospital shown on the chart), when his condition became worse. The temperature reached 107° F., he was toxic, irritable, semidelirious, and showed some nuchal rigidity. The knee-jerks were inactive, but Kernig's and Brudzinski signs were negative. Nothing abnormal could be found on examina-

<sup>1</sup> Post-graduate Clinic.

tion of the lungs. He was seen again with the otologist, who confirmed the negative ear and mastoid findings. Another



pediatrician was called in for consultation, who, likewise, could find nothing abnormal in the lungs. In view of the developing signs of meningeal irritation and negative pulmonary findings

it was decided to take the youngster to the hospital for lumbar puncture. This was done late in the afternoon, and the fluid obtained was clear and without an increase in the number of

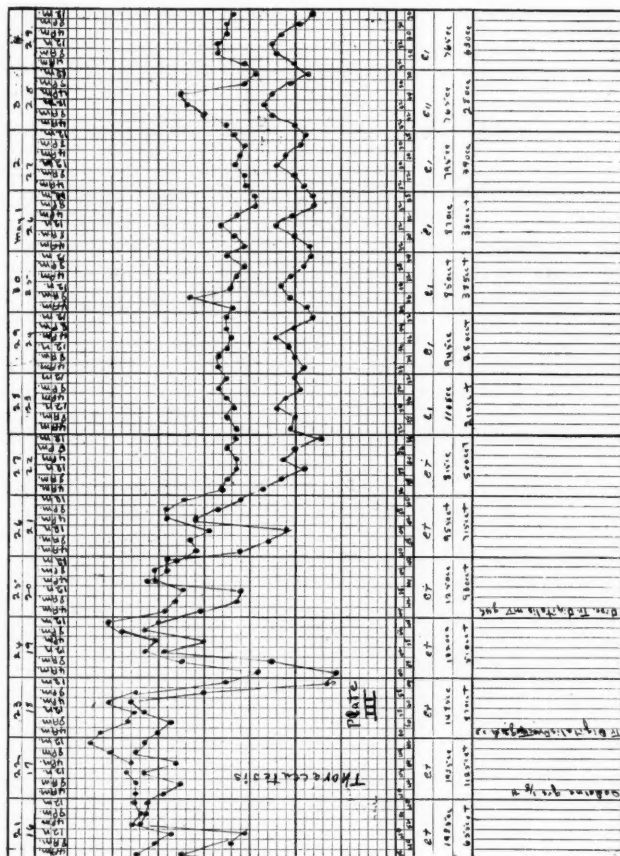


Fig. 264.—Chart of patient with lobar pneumonia. The onset occurred two days before this chart was started at the hospital.

cells. The temperature continued high—104° to 105° F.—that night and the following day, but the signs of meningeal irritation became less marked. The following morning, the fourth day of the disease, the lung findings were negative and no shadow

was found with a fluoroscope. On the following day a shadow was found on the left side extending into the axilla (Fig. 265), but it was not until that evening that the ordinary signs of a pulmonic consolidation were found at the angle of the left scapula by physical examination. On the day before the signs in the lungs developed the abdomen became taut and slightly distended, the legs were drawn up, and the child complained on any attempt to palpate. The question of peritoneal irrita-

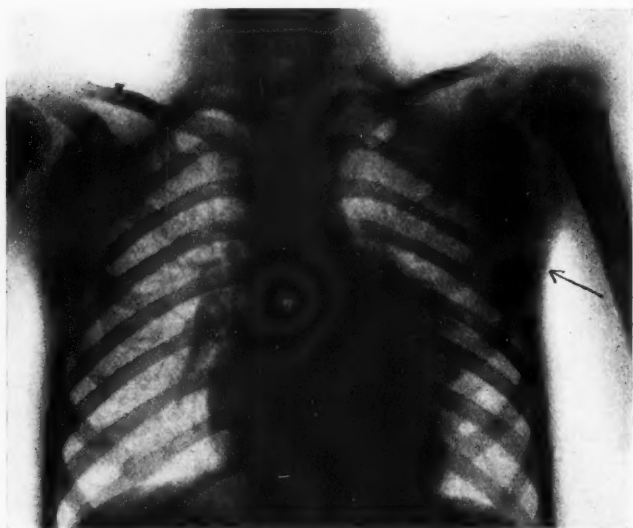


Fig. 265.—4/9/23: Early shadow left side.

tion was raised, but it was found that the abdomen could be palpated when the child was asleep and that actual muscle spasm was not present. These signs of peritoneal irritation disappeared inside of thirty-six hours.

Before relating the further course of the child's illness I wish to discuss with you three questions which are brought up by the history of the case so far as these three are interrelated. They are:

1. The late development of pulmonary signs.
2. The question of meningeal irritation and meningitis.
3. The question of peritoneal irritation.

1. **Delayed Development of Physical Signs.**—The late development of pulmonary consolidation with physical signs obtainable by auscultation and percussion is not at all uncommon in lobar pneumonia in childhood. In fact, we often make a diagnosis by the sudden rise in fever, slight cough, type of breathing, and absence of other causes twenty-four or more hours before alteration in auscultation and percussion of the lungs is found. It is not usual to see so late a development as occurred in this case, but we have records of a number of cases in which the signs did not develop until at or near the crisis. It is usually possible to make an accurate diagnosis in these cases by the course of the fever, the rapid respiration, the "inverted" type of breathing in which the pause occurs after inspiration instead of expiration, the high leukocyte count, the playing of the alæ of the nose taken in combination with the absence of other findings of a causative nature. Where signs of meningeal or peritoneal irritation are present, however, the diagnosis must be carefully guarded.

The old explanation was that these were "central pneumonias," and this explanation has sufficed for years. The use of the x-ray and fluoroscope in internal medicine has shown us that this is not the correct explanation, but that in fact these pneumonias are peripheral pneumonias. In 1916 Mason found that in children an x-ray taken before the development of bronchial signs frequently showed a triangular shadow in the roentgenogram with the base at the periphery (or pleural surface) and the apex pointing toward the hilum. When the shadow reaches from the periphery to the hilum the bronchial signs develop. This has since been confirmed in many clinics. Very often this shadow will be found for some time before definite signs can be found on physical examination, and hence the x-ray forms one of our most valuable aids in the diagnosis of pneumonia and should be used routinely in all questionable cases. When a child can be examined under ideal conditions an

impairment of resonance or some degree of suppression of breathing can at times be made out, but often this is impossible on account of the toxic, irritated, fretful condition of the child being examined. Figure 265 shows an early shadow, not so clear cut as is usually seen, but it must be remembered that in this case our x-ray findings were negative through the fourth day of the disease.

This late development of consolidation which one sees in children is a clinical confirmation of the fact that lobar pneumonia is a pneumococcemia. The sudden recovery that occurs with the crisis is an overcoming of this infection, and one frequently sees the consolidation persist in the lung for days after the crisis has taken place.

## 2. The Question of Meningeal Irritation and Meningitis.—

Fortunately meningitis associated with pneumonia is rare, while meningeal irritation with which it may be confused is not uncommon. But we are not so much interested in the question of a complicating meningitis which usually occurs late in the course of a pneumonia and associated with empyema, as in the question that arose in this case between the diagnosis of pneumonia with meningeal irritation on the one hand and a primary meningitis on the other. From the first we were of the opinion that we were dealing with a pneumonia, but on the second day, when no signs could be found in the lungs and meningeal irritation developed, serious consideration had to be given to the question of meningitis. A possible decision could be reached in no other way than by lumbar puncture. Influencing us to consider the possibility of meningitis were two factors related in the history: first, the presence of an otitis media the previous week, and, second, the onset with a convulsion which is by no means common—less than 10 per cent.—at the onset of a pneumonia in childhood. The only objection to a lumbar puncture was the more or less theoretic possibility of infecting a sterile spinal fluid with pneumococci from the blood-stream. Against this had to be balanced the loss of valuable time in case our diagnosis of pneumonia was wrong and we were dealing with a meningococcal meningitis. The result I have given you



in the history. Meningeal irritation or meningismus or "serous meningitis," as it was called in the past, is quite frequently seen in the course of a pneumonia, and it is rarely ever necessary to perform a lumbar puncture for diagnostic purposes. The irritation usually occurs fairly early at the height of a toxicity, as it did in this case, whereas a complicating meningitis is almost always associated with a complicating otitis media or empyema and develops late.

3. **The Question of Peritoneal Irritation.**—I consider this the most important question of differential diagnosis which one meets with in the lobar pneumonia of childhood. It is not at all uncommon to see a child whose appendix has been taken out and to hear from the parents the story that just after the operation the child developed pneumonia. Of course, the truth was that the child had had a lobar pneumonia with abdominal symptoms that had been mistaken for appendicitis, but I have no criticism of the physician in charge of such a case because it is one of the most difficult, if not at times impossible, of differential diagnoses, and I do not know of a pediatrician of standing who has not frankly been willing to admit that he has made this error at some time, and many of us admit to having made it more than once. If I never make it again I will consider myself lucky. My first experience a number of years ago was unusual in that the question came up twice in twenty-four hours with the same surgeons. Our error was 50 per cent. This made a strong impression upon me and I have always been interested in the problem. The problem presented is this: A child in good health is suddenly seized with vomiting and pain in the right side of the abdomen. The fever is found elevated several degrees. On examination, a resistance, but very little muscle spasm is found. Frequently the child is too sick and irritable to allow of a satisfactory abdominal or pulmonary examination. We are dealing with either an appendix or pneumonia. As you know, the signs of appendicitis in a child are frequently vague and uncertain. From 75 to 85 per cent. of the children who are admitted to the Children's Hospital for appendicitis either have an abscess with localized peritonitis or a general per-

itonitis, which simply goes to show the difficulty in making an early diagnosis in the average case of appendicitis in childhood. On the other hand, pneumonia frequently is ushered in with vomiting and if the consolidation starts at or near the pleura covering the diaphragmatic surface of a lower lobe the pain is referred to the abdomen. With a young child who cannot localize pain accurately, or when the pneumonia causes a general irritation or excitement, abdominal rigidity is easily produced or simulated. If in these cases, as frequently happens, physical signs of a pneumonia cannot be made out, the question of diagnosis is an important one. A very high fever and leukocyte count point to a pneumonia. An absence of muscle spasm elicited by tapping the right side of the abdomen, even if the abdominal wall is held rigidly, is against appendicitis. A fluoroscopic examination of the chest in which a shadow was found, although physical signs were absent, has settled the diagnosis in several cases. This is one of the most important methods of differentiation and should be used in every questionable case. I recall one child who was saved from operation by the finding of a slight suppression of respiration over the lower right lung, but in some cases all signs fail and the diagnosis is uncertain. The question then comes up as to what is best to be done. If we do nothing and the pneumonia develops, all is well and good. If we procrastinate, and it is appendicitis, the child's life may have been jeopardized by the delay. What we have to do is to weigh the question as to whether the seriousness of delaying an operation for appendicitis is outbalanced by an unnecessary abdominal operation in an early pneumonia. Experience gained from operating upon cases in which a mistake in diagnosis has been made has shown us that the course of the pneumonia is not influenced by the abdominal incision. My own practice is to operate if the symptoms seem to be more in line with an appendix than a pneumonia, and to wait if vice versa. If, however, as frequently occurs, it is a 50-50 choice, I believe in putting the proposition and difficulty squarely before the parents and advising them the danger of a delayed operation for appendicitis in a child is greater than a rapid exploratory

abdominal incision with a developing pneumonia and a normal abdomen. While you will be criticized by the laity and the friends of the patient if the operation was unnecessary, you will always have the feeling that you did the right thing by the child.

To continue with the history of the case: The meningeal and peritoneal symptoms became less marked, but the child

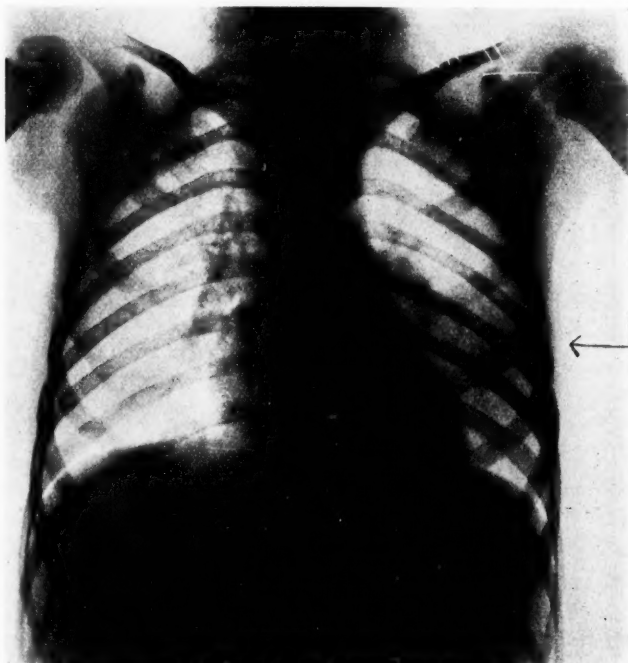


Fig. 266.—4/20/23: Shadow on left side.

was unusually sick or toxic. Along about the eighth or ninth day the temperature began to fall by lysis and the expected crisis did not take place. The signs of consolidation persisted at the angle of the left scapula. On the twelfth day the right ear started to discharge, but the temperature on the succeeding days continued to go higher. We began to suspect empyema,

but the physical signs remained unchanged. On the fifteenth day another fluoroscopic examination was made and a plate taken (Fig. 266). The actinographic laboratory report was "very suspicious of fluid." The plate shows the shadow on the left side. That night the temperature fell to normal for the first time, but to our distress started to climb again the following

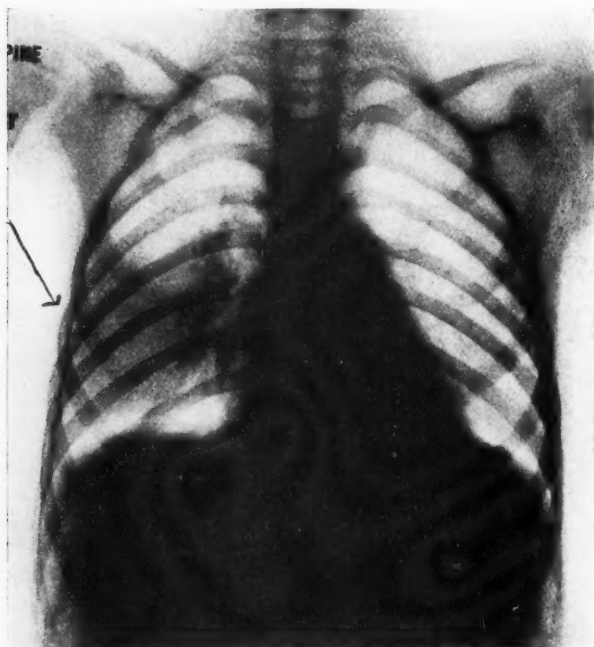


Fig. 267.—4/23/23: Shadow on right side. Left side shadow disappeared.

day, and so the next morning, the seventeenth of the disease, a thoracentesis was done. I made several punctures over the area of physical signs on the left side, but obtained nothing but a little blood. That evening some dulness and bronchial breathing was heard for the first time on the *right* side in the axilla. A roentgenogram the following day (Fig. 267) showed a shadow on the right side. Thus after a long-continued pneumonia on

the left side a new process on the opposite side developed which accounted for the sudden rise and high fever from the sixteenth to eighteenth day. This lung cleared rapidly and at the same time resolution took place in the left lung. The temperature fell by lysis and from the twenty-second day on there was no further rise in temperature. During convalescence albumin and a few casts persisted for several weeks, but soon disappeared. The youngster was quite sick and toxic throughout the entire course. He had had three weeks of a severe toxemia, such as only a child can withstand.

The four additional points raised in this case which I briefly wish to discuss are:

4. Empyema.
5. Multiple or secondary consolidation.
6. The prognosis and morbidity in lobar pneumonia in childhood.
7. Treatment.

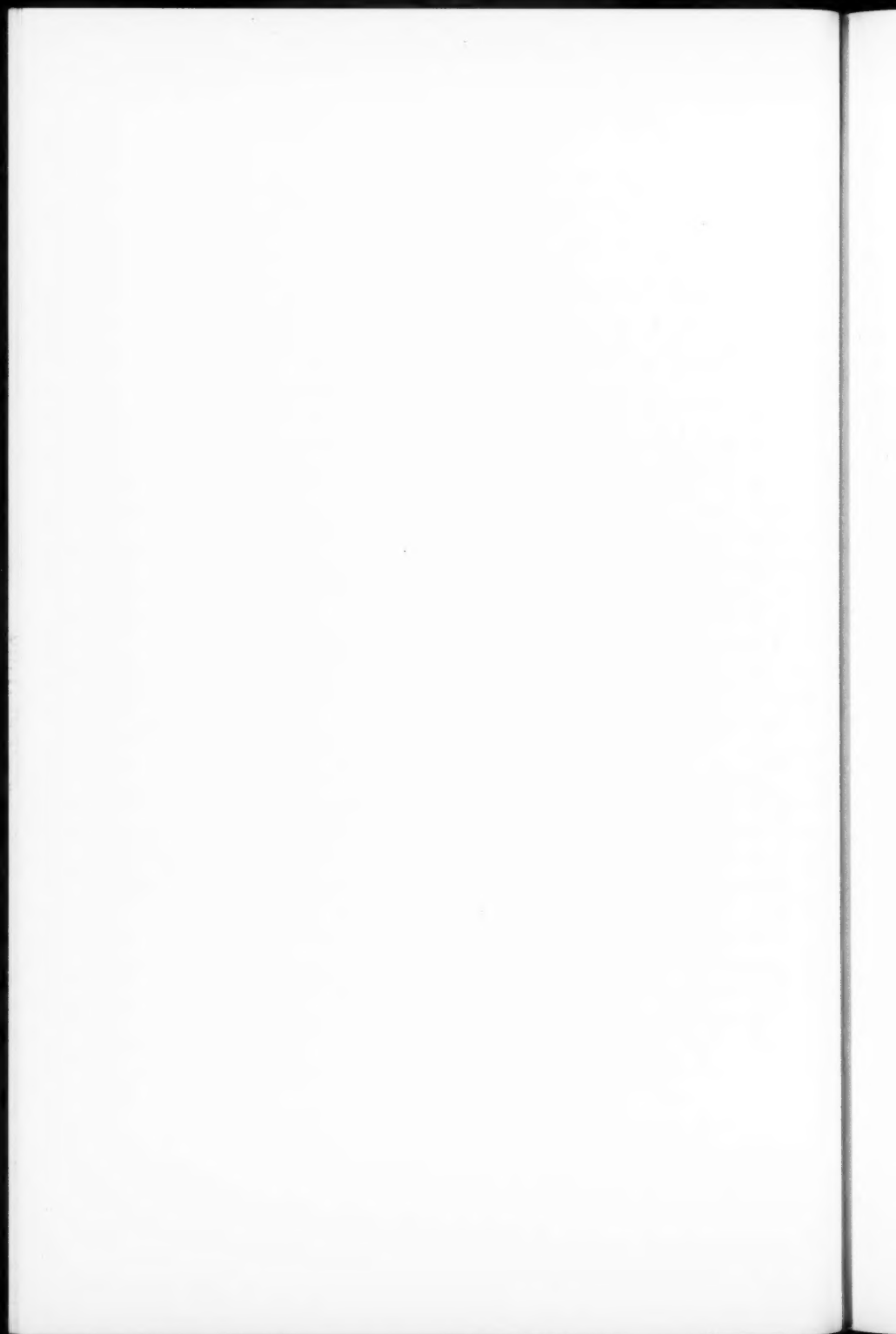
4. **Empyema.**—The development of a purulent pleurisy is, as you know, not uncommon in children with pneumonia. It is seen in about 12 per cent. of the cases in childhood as contrasted with 2 to 3 per cent. in adults. In nearly all of these cases the pneumococcus is the organism present. As a rule the empyema begins to manifest itself a day or so after the crisis with the development of an irregular temperature, but occasionally it is coincident with the pneumonia, and one first suspects it when the expected crisis does not take place. Unless considerable fluid has collected or the empyema has persisted for some time the physical signs do not differ much from the signs of an unresolved pneumonia. The x-ray may give valuable information, but frequently these findings are indefinite early in the disease. Thoracentesis, if pus is obtained, is the most certain method of diagnosis. Sometimes we fail for some reason or another to hit the pus, and repeated punctures are necessary. In this case had we not found the pneumonia on the opposite side the night after thoracentesis we would have made repeated punctures if the temperature had remained elevated. I recall a case that was punctured eight times before

pus was obtained. The diagnosis of empyema is so relatively easy that we are often surprised to see children sent in for diagnosis and treatment who have had pus present for weeks. In young infants the prognosis of empyema is not good as a result of the severe drain of the pneumonia and subsequent pleural infection upon the nutrition. Older children make excellent recoveries as a rule. Aspiration and closed drainage with suction have considerably lessened the mortality from empyema as contrasted with open drainage as used by the surgeon a few years ago.

**5. Multiple or Secondary Consolidation.**—This is much less common than empyema. Double pneumonias are often seen, but the "wandering" type is fortunately less frequent. It naturally adds to the gravity of a case. If the temperature continues or remains high after the time of crisis and physical signs persist at the site of the consolidation one would naturally suspect empyema at first. Plate II, taken on the fifteenth day of the disease, shows no evidence of a pneumonia on the right side, while Plate III, taken three days later, shows a well-developed consolidation.

**6. Prognosis.**—Although there is no other disease of childhood in which the patient appears more toxic and sick, the mortality of lobar or croupous pneumonia is low. Instead of the 25 to 30 per cent. mortality in the adult, mortality with children is around 3 per cent., and so even in the sickest cases we can hold out a good prognosis to the anxious parents. I have no hesitation in saying that an adult as sick as this child would have had but a slight chance of recovery. The factor lies in the strength of the child's heart which has not been insulted through years of repeated infections, hard work, bad food, alcohol, and the like, which we know tend gradually to lower the reserve power, or, as Meltzer so aptly termed it, the "factor of safety." It is this low mortality rate seemingly which explains the frequency of empyema in children. Probably the incidence of empyema would be the same in the adult if the severe cases did not die before the empyema had had time to develop.

7. **Treatment.**—We have as yet no satisfactory specific method for the treatment of lobar pneumonia. As stated above, nearly all cases in children get well, as the disease is self-limited. The most we can do is to protect the child from wearing himself out through lack of food, fluid, and sleep. Consequently, good nursing is essential. From the first fluids were forced. Our chief difficulty lay in the toxic irritable condition of the child, who threw himself about in a semi- or actual delirium. I have seen a number of children allowed to exhaust their strength in this way when every ounce of it is needed to combat the disease. I feel that rest is the most essential factor in the treatment, and so, as you will see by reference to the chart, an opiate (codein gr.  $\frac{1}{6}$ ) was freely used in the early stages. As the early toxicity decreased this was discontinued. I feel an opiate is perhaps our most valuable drug. In the early stages the pulse was rapid and at times weak, so digitalis was given over the fourth, fifth, and sixth days. It was not necessary to use a more rapidly acting cardiac stimulant at any time in this case. Fresh air, fluids, food, and rest constitute the chief essentials of treatment, and the majority of our cases go through their entire course and convalescence without any medication.





## CLINIC OF DR. PHILIP C. JEANS

ST. LOUIS CHILDREN'S HOSPITAL

### DIPHTHERIA

THE patient before you, a girl of ten years, has typical faucial diphtheria of two days' duration. The throat culture is positive. The feature of interest is that one week ago she was given a prophylactic injection of 1000 units of diphtheria antitoxin. Her sister, eight years old, contracted diphtheria nine days ago, and seven days ago received intramuscularly 10,000 units of antitoxin. The sister died yesterday. In the presence of virulent and extensive diphtheria, it is possible for sufficient toxin to be elaborated, absorbed, and fixed in the body in two days so that no amount of antitoxin would prevent death. In the absence of further evidence such an explanation of the sister's death might be accepted as the true one. However, it is inconceivable that a child of ten years could develop clinical diphtheria five days after receiving 1000 units of antitoxin. It seems to me that but one inference is possible to explain the development of diphtheria in this patient, and that is that the antitoxin had lost its potency. The chief factors in loss of antitoxic potency are aging and heat, particularly the combination of these two factors. The antitoxin used in the patient and her sister was purchased from a small neighborhood drug store by the family physician. It has been my observation that refrigeration of biologic products in many such stores is very poor. Accepting these premises, the obvious lesson to be derived from this experience is one of care in choosing a source of supply for antitoxin and other biologic products.

Another factor which should be mentioned in connection with this case is the duration of immunity conferred by the

injection of antitoxin. Passive immunity so obtained lasts in the neighborhood of three weeks following the first injection of antitoxin. Following the second injection of antitoxin given a few weeks after the first injection immunity sufficient to protect lasts approximately only ten days. With each succeeding injection the antitoxin is somewhat more rapidly destroyed in the body. These facts could scarcely explain the development of diphtheria in this patient, since she has never had antitoxin before, and the interval between the antitoxin injection and the development of diphtheria was only five days. The facts just enumerated are of importance, however, in other respects. They explain the occasional or rather rare relapses of diphtheria, and also make clear the fallacy of using antitoxin as the sole means of controlling an epidemic of diphtheria. We have observed instances of relapse of clinical diphtheria in patients who continued to harbor the diphtheria bacillus after the disappearance of their passive immunity. One patient was observed to have several successive relapses of mild degree. In the management of an epidemic of diphtheria in a group or an institution it is obvious that, if the sole measure taken is administration of antitoxin to each of the group, the epidemic is only postponed for about three weeks, and at the expiration of that time is likely to continue as before.

A question constantly arising in relation to antitoxin is the safety of administration. That deaths occur as a direct result of the foreign protein of antitoxic serum there can be no doubt. It has been estimated that one death occurs to each 70,000 serum injections. Fortunately, it falls to the lot of but few physicians to witness such an event. The general mortality of diphtheria of all varieties and at all ages is in the neighborhood of 25,000 to each 70,000 when antitoxin is not used. The relative safety of antitoxin as compared to diphtheria disease is tremendous. The danger of giving antitoxin to patients who have previously received a serum injection is frequently stressed. However, with but exceedingly few exceptions, all of the recorded deaths charged to antitoxin have followed the first injection. Repeatedly have I given and seen given second and third injec-

tions of antitoxin without serious ill effect, even though sufficient interval had elapsed for the development of anaphylaxis. As far as my own observation goes, the danger from a second injection of antitoxin at any interval is so slight as to be entirely negligible. Unfavorable symptoms are seen more frequently after intravenous administration than after the use of other routes. Such more or less serious symptoms (none fatal) as we have observed after intravenous administration of antitoxin were not of the nature of specific reactions to foreign protein, but were rather those of shock. Such a reaction may occur after any intravenous serum injection, whether it be the first, second, or tenth, and whether or not the patient is sensitized to horse-serum. When serum is given intravenously exceedingly slow administration in the beginning will help to avoid serious results. In one condition particularly should one be guarded in administering horse-serum. That condition is asthma, especially should the asthma be due to horse protein. In asthma or any other condition in which the physician desires to be particularly careful the serum should be given in divided doses, the first injection being quite small. One very good method is to give  $\frac{1}{4}$  to  $\frac{1}{2}$  c.c. (4-8 minims) subcutaneously. Three or four hours later, if no symptoms have occurred, the full therapeutic dose is given. Another method is to start with  $\frac{1}{10}$  c.c. (or 1 minim) intramuscularly. If no symptoms occur the injection is repeated each twenty to thirty minutes, increasing the dose each injection by  $\frac{1}{10}$  c.c. until the full dose has been given or symptoms elicited. Moderate asthmatic symptoms may be controlled by adrenalin or atropin, and these should be at hand for emergency use. These same remedies are useful in serum shock mentioned a moment ago.

The second patient I wish to show you is a girl of ten years. Five days ago she came home from school with a chill and a sore throat. Twenty-four hours later a physician was called. Exudate was present on the tonsils and diphtheria was considered as a possible diagnosis. A culture was taken and was reported the next day as negative for diphtheria bacilli. A second culture taken forty-eight hours after onset also was re-

ported to show no diphtheria bacilli. Because of these two negative cultures the physician considered the condition as one other than diphtheria, probably a streptococcus pseudomembrane. No antitoxin was given. Because of increasing prostration the patient was brought to the hospital last night, four days after onset. Because of the clinical appearance antitoxin was given at once, 5000 units intravenously and 10,000 intramuscularly. A culture taken last night shows diphtheria bacilli this morning. The patient now is obviously moribund. She lies quietly, has a poor color, slightly cyanotic, and the pulse is not perceptible at the wrist. Temperature 103° F. The throat is dry, tonsils swollen and streaked with dirty grayish-white pseudomembrane. The left heart border is 1 cm. outside the left nipple. The heart sounds are of poor quality, indicating loss of muscle tone. The first sound is weak. The heart sounds are very irregular, a slow period with queer extra beats, then a hurried period. There is great weakness of the whole body. The diagnosis is pharyngeal diphtheria and myocarditis as one of the toxic effects. It is an example of failure of early recognition which was due to too much dependence on cultures. Whenever an acute illness strongly resembles diphtheria it is good policy to treat it as for diphtheria and to make the diagnosis afterward. In carrying out such a policy sometimes antitoxin will be given unnecessarily. As pointed out a few minutes ago, the danger from antitoxin is exceedingly small, while that from diphtheria is great. The lesson to be derived from this case is obvious. The question arises, Why were the first cultures negative? This is not easy to answer in a definite manner. It is a fact that many times in true diphtheria early cultures, as taken, fail to grow the diphtheria bacillus. The most probable explanation is the location of the diphtheria bacilli beneath the surface of the membrane, especially early in the disease. Cultures taken deeper than the surface will show diphtheria bacilli more uniformly, as also will cultures taken later in the disease.

The third patient is a boy of five years. Twelve days ago he developed a sore throat with fever. The appearance of the

throat is said to have been similar to follicular tonsillitis, and that diagnosis was made by the physician who was called. After five days the throat had assumed an appearance which prompted the physician to diagnose diphtheria and to administer antitoxin. No culture has been taken. It is of interest to note that the sister of this patient became ill with a sore throat nineteen days ago. In the sister also the clinical appearance is said to have been that of typical follicular tonsillitis and remained so. No cultures were taken and no antitoxin given. The sister was recently admitted to this hospital and now has acute myocarditis and multiple neuritis presumably the result of diphtheria toxin. Cultures from her throat show diphtheria bacilli. In the case of the patient before you 3000 units were given subcutaneously five days after the onset, and late the same night 10,000 units more were administered. Because he was not progressing very well 5000 units more were given seven days after onset. Five days ago and seven days after the onset the patient was admitted to this hospital. At the time of admission he was quite prostrated and somewhat stuporous. He had a bloody nasal discharge. The pharynx was covered with dirty gray necrotic material. There was moderate laryngeal involvement. But slight evidence of myocarditis was present. On admission to the hospital he was given 15,000 units of antitoxin, half intravenously and half intramuscularly. His temperature was 100° F. on admission and has not been above 100° F. since. He has improved steadily until today. The throat swelling has disappeared, he became able to swallow with ease, and has been much more alert mentally. The chances for recovery seemed to increase. Today the general appearance became much worse. General weakness is greatly increased. The left heart border is 1 cm. outside of the left nipple and the heart sounds are faint and irregular. In addition to myocarditis the electrocardiogram shows a right bundle branch block. Vomiting is present. The liver is distinctly enlarged. With such marked myocarditis and decompensation the prognosis is extremely bad and death seems imminent. The essential indication in treatment now is rest and quiet, just as absolute as

possible. Such rest should be assured by adequate doses of morphin.

Several lessons are to be learned from the case of this boy and that of his sister. It is important to realize that true diphtheria of the tonsils in its early stages not infrequently presents the clinical features typical of follicular tonsillitis. In a few instances it may retain these clinical features throughout its course. For this reason it is advisable to make cultures of all sore throats regardless of the clinical impression as to the diagnosis. In the preceding case it is observed that too much reliance on negative laboratory findings may be a serious mistake, and in such a case as the preceding one the clinical impressions should have the most weight. But the value of positive laboratory findings is quite different from that of negative ones. When a clinically follicular tonsillitis is associated with cultures showing diphtheria bacilli there can be no question as to the proper therapeutic procedure. Antitoxin should be given.

Another important point in the treatment of diphtheria is suggested by this case. That point is the method of administration of antitoxin. That the route of administration is important is not sufficiently realized or emphasized. Nor is it generally enough realized that a very marked disadvantage attends multiple doses. In this case multiple doses of antitoxin were given and the first ones by the subcutaneous route. The damage done by diphtheria is caused almost exclusively by diphtheria toxin. The diphtheria bacillus without its toxin is quite harmless. Toxin is absorbed from the site of the disease and is distributed by way of the blood and lymphatics throughout the body. The chief object in therapy is to reach that toxin with antitoxin at the earliest possible moment. It is obvious that this result will be accomplished most rapidly when antitoxin is given intravenously, and this route should be used in all cases in which the patient is seen late and in the more severe types seen early. Because of the rather unpleasant reactions often occurring after intravenous antitoxin, other routes are chosen for the milder cases early in the disease. When anti-

toxin is given subcutaneously the maximum concentration of antitoxin in the blood is not reached for about three days, while when given intramuscularly the maximum blood concentration is reached within twenty-four hours. Antitoxin may be given intramuscularly with no greater difficulty than subcutaneously. The difference in speed of absorption by these two routes is so great that in many instances it may determine between life and death for the patient. Giving antitoxin subcutaneously is practically equivalent to postponing antitoxin administration for two or three days depending on whether it is compared to the intramuscular or intravenous route. The subcutaneous route is the route of choice for prophylactic injection, but for therapy this route should never be used. Antitoxin given intraperitoneally is said to be absorbed more rapidly than when given intramuscularly, and with no more reaction. This route has not yet been used in a sufficient number of cases to demonstrate its safety, though there are no *a priori* grounds for assuming it unsafe.

Three units of antitoxin will neutralize in the test-tube sufficient toxin to kill a man weighing 150 pounds. Several thousand times this amount is used in practice. Such large doses are used because of the slow diffusion of antitoxic serum through the body and the "pressure effect" of large amounts speeds up diffusion. A large dose is used also in order to have available a considerable excess of antitoxin in whatever part of the body toxin is to be found. Such a large excess is desired in the hope of dissociating the union of toxin with body tissues when the toxin has not yet had time to become completely fixed in the tissues. When antitoxin has been given in the first dose in sufficient amount to have an excess everywhere available it is obvious that a second dose is useless. If a certain amount of antitoxin is necessary for the recovery of a patient, and this amount is given in two or more doses separated by an interval, valuable time has been lost equal to the interval between the first and last dose. This lost time may be sufficient in certain instances to determine between life and death of the patient. Many animal experiments could be cited to show that a single



large dose is the most effective treatment. In experimental animals a proper single dose will save life uniformly, when under the same conditions much larger amounts given in divided dosage uniformly fail to save life.

The sister of the patient before you continues to harbor the diphtheria bacillus in her throat. It is nearly three weeks since the onset of her diphtheria. Many patients will be free from diphtheria bacilli before the end of three weeks, though three weeks is not an uncommonly long time for these organisms to be found. When a patient continues to have diphtheria bacilli in the throat for unusually long periods, it has been found that there is usually some pathologic condition in the nose or throat. The most frequent pathologic condition is hypertrophied tonsils and adenoids. It has been our experience that the most uniformly effective method of terminating a chronic carrier state after diphtheria is surgical removal of the tonsils and adenoids. But few cases fail to respond to this treatment, while the results with gargles, washes, sprays, and other local applications of any nature which we have tried have been very disappointing.

The 3 cases I have shown you today have been selected from the material in the wards because they serve to illustrate common mistakes in the diagnosis and treatment of diphtheria. I have endeavored to point out these common errors and their remedy.



## CLINIC OF DR. JOHN ZAHORSKY

BETHESDA HOSPITAL

- I. THE MOUTH-AND-HAND SYNKINESIA.
- II. ERYTHEMA NODOSUM IN AN INFANT.
- III. RECOVERY FROM EXTREME MARASMUS.

### I. THE MOUTH-AND-HAND SYNKINESIA

THE first two children presented are not very sick, in fact, one of them is perfectly well, but I bring them before you to exemplify a new sign. I call it the mouth-and-hand synkinesia. My attention to this phenomenon was called first by Dr. E. W. Saunders, of St. Louis, and we often call it Saunders' sign. It is not a reflex, but an associated movement, technically called synkinesia.

This little boy is five years old, and presents no abnormality at present except a slight coryza. He is a bright, active child. I will ask him to open his mouth, but you keep your eyes on his hands especially.

To the child: Open your mouth. Open it wide as you can.

You will observe that with the act of opening his mouth very wide there is an associated movement in his hands. The hand is opened, the fingers are extended and separated, and the thumb is extended almost at a right angle to the wrist.

This is the mouth-and-hand synkinesia.

A better way to elicit this phenomenon is to sit in front of the child and very loosely hold his hands in yours. Now, ask him to open his mouth widely. You thus perceive this extension of the fingers and also feel the muscular contraction accompanying the act. The synkinesia is especially striking in the extension of the thumb, the finger extension is generally less marked.

I have studied this associated movement for many years in hundreds of children. It has been found that the phenomenon

disappears gradually as the child grows older, usually it is not present after twelve years of age. Many children at the age of nine or ten do not respond to this test. In young healthy children under seven years of age its presence is characteristic of the healthy child. It is often absent in feeble, delicate children or in some acute illness, as pneumonia. Thus far, it can be stated, its occasional absence even in the young child has no special clinical importance.

Now, I will show you another child.

This girl is seven years old. As she stands before you, observe the irregular movements in her face, shoulders, and arms. This is especially marked on her left side. On asking her to talk, it is found that she speaks with a hurried, irregular speech. On watching her respiration, its irregularity and jerking character becomes evident. She has been nervous for six weeks. No definite cause could be made out. She has had no marked sore throat. Her tonsils and adenoids were removed two years ago. She has had no fever. The heart sounds are perfectly normal.

This is evidently a mild case of chorea minor. She is brought before you to demonstrate the peculiar and characteristic change in the mouth-and-hand synkinesia. On requesting her to open her mouth very wide, you will notice that the response in the hands is weak. The extension of the thumb on the right side is slight, but a greater extension is present on the left hand, but this is associated with a singular jerking of the hand on the wrist. This is quite different from the steady extension of the thumb and fingers as shown by the other child.

This sign has a clinical value in differentiating certain forms of tic, or habit spasms, from chorea. In the former class of cases the mouth-and-hand synkinesia is strong and steady, in the latter disease weak and jerking. Therefore, in all cases of "nervousness," we make this test, and the quality of it has often assisted in making a diagnosis.

I have found no references to this phenomenon in the medical literature. Griffith, in *Diseases of Infants and Children*, makes this statement: "I have frequently found that the grasp-

ing of the wrist as though the pulse were being felt, or the requesting of the patient to put out the tongue, will reveal the condition. At the wrist there is felt slight twitching of the muscles, while the tongue is often suddenly jerked back into the oral cavity before the order is given to close the mouth."

He does not, however, recognize that the opening of the mouth and twitching of the wrist is an associated movement.

## II. ERYTHEMA NODOSUM IN AN INFANT

The next case to be presented is a rare disease in infancy, and has given us some concern as to the etiology and prognosis.

This girl is seventeen months old. It is the only child of healthy Jewish parents. No history of tuberculosis, nervous disease, or diabetes could be found on inquiry among the near relations.

The baby was born at term, seemed healthy in every way, and was breast fed for one year. Supplemental feeding with cow's milk began at six months of age; to this a mixed diet of cereals, vegetables, and fruit was added after the seventh month. When she was a year old she suffered for two weeks from a respiratory infection, angina, coryza, and bronchitis. In August of this year she had an attack of enteritis. Diarrhea with mucus and microscopic pus in the stools persisted for ten days or more. She slowly recovered, but the mother thinks she has not been exactly well since this illness.

One week ago she became suddenly ill with high fever; when first seen she had a temperature of 104° F. She vomited once only. She had no cough, seemed to have no pain, and the bowels were constipated.

The physical examination revealed no definite abnormality anywhere.

The fever ran an irregular course, but remained high for several days. On the third day a thorough examination revealed no infected focus anywhere. The tonsils were slightly congested, the mouth healthy, the ear-drums were pearly, no cervical glands enlarged. Heart and lungs seemed normal. Nothing was made out in the abdomen; the spleen was not pal-

pable. The extremities were not especially tender; no Kernig, no rigidity of the neck, no Brudzinski. The stools seemed constipated and microscopically showed no pus-cells.

I suspected a pyelitis, but the urine contained no pus-cells, only a faint trace of albumin. I suspected that it was a case of roseola infantum and the child would break out with a morbilliform rash on the following day. But the leukocyte count was nearly 13,000; that is, there was not a leukopenia so characteristic of roseola infantum.

On the fifth day the baby did have an eruption, but the fever did not drop by crisis and the efflorescence was not morbilliform. The eruption consisted of macules about the size of a split pea scattered over the arm and forearm, also on the legs, thighs, and a few around the hips. These lesions were bluish red and some of them did not entirely disappear on pressure. There was no skin lesion on the trunk or face. The joints were not swollen.

On the following day it was observed that the lesions on the extensor surface of the leg had become the size of a bean or hazel-nut and very dark bluish in appearance.

This is the eighth day of the disease. You still see the macules scattered over the extensor surfaces of the arm and leg. Notice the dark bluish character of the lesions over the tibia. On palpation they feel hard, like a nodule in the skin. There are four nodules on one leg and five on the other. The erythematous spots elsewhere do not feel nodular.

We are justified in calling this erythema nodosum, a very rare disease in infants.

The disease occurs most frequently in children about the age of puberty, or young adults.

As tuberculosis has been given as one cause, a von Pirquet was made two days ago. You see the skin reaction is negative on the third day after the test was made.

**Note.**—The fever disappeared gradually, the nodules persisted for several days after the temperature became normal. The baby, except for a pallor, seemed perfectly well after three weeks. The treatment throughout was symptomatic.

### III. RECOVERY FROM EXTREME MARASMUS

There is nothing rare or unusual about the third case which is presented. It is a case of extreme infantile atrophy, or marasmus, arising rather acutely. It is shown especially for the purpose of demonstrating a new treatment which I have adopted. The principle is not new, but the method employed is somewhat different from the accepted form of therapy. In order to appreciate the problem we will first study the case.

The little patient is a girl three months old. The parents live in a small town in Illinois, and this baby was taken to St. Louis and brought to my office yesterday. She was at once sent to the Bethesda Hospital in what seemed to be a dying condition.

The family history gives nothing of importance. The baby was one of twins, her sister died about two weeks ago. The baby was nursed for one month, when, on account of scantiness of mother's milk, she was placed on the bottle. Soon after birth the twins contracted whooping-cough, as a result of which one baby died two weeks ago. The babies were fed a mixture of cow's milk and oatmeal gruel. During the illness with whooping-cough our little patient continued to lose in weight, or at least made no gain. One week ago a diarrhea supervened, the weight rapidly decreased, and she sank into an extreme state of inanition.

**Examination.**—Notice the extreme atrophy, the integument clings to the bones. The skin has an ashen gray color. The extremities feel cold. The eyes are sunken, the lids do not wink. The eyeballs are not exsiccated, however. The skin shows no infection. On pinching up the thin skin anywhere you will observe how slowly it returns to its normal smoothness, its elasticity is markedly reduced. When you compress one of its fingers you find no increased congestion of the nail, showing that there is very little peripheral circulation in the capillaries. A prick with a fine needle brings out not a single drop of blood.

Examination of the mouth, throat, and ears shows no evidence of acute infection. A few mucous râles are heard over both

lungs. The heart sounds are rather slow (100). Liver and spleen are not enlarged. The child lies in a semistupor, but coughs occasionally. She refuses food.

Blood examination reveals a leukocyte count of 12,000. Rectal temperature 98° F., weight only 2470 grams.

The stool examination gave no evidence of a serious enteritis, as only a few cells were found under a microscope.

Diagnosis: Marasmus.

Now let us consider the therapeutic problem before us.

First, the baby suffers from extreme starvation, all the tissues are wasted, no reserve food anywhere, and the blood volume enormously reduced. The blood volume is so small that little or no blood enters the peripheral circulation. Probably a less amount also enters the internal organs and, consequently, the digestive function is materially impaired; at any rate, clinical experience abundantly proves that a great reduction in blood volume is followed by a great weakening of the digestive process. The capillaries of the gastric and intestinal mucous membrane are not thoroughly filled, some may be entirely empty. By analogy we assume that the accessory glands of the digestive organs are also depleted. Our problem then is to try to nourish a baby almost dead of inanition who has a feeble digestive capacity.

I am inclined to think there is no extensive disease of the intestine present in this case. If a severe inflammatory lesion is present in the small intestine in a case of extreme atrophy, we are almost powerless to avert the fatal outcome. Here we assume that the stomach and intestine are still intact or at least not seriously damaged.

The principal problem, then, is to increase the blood volume. This cannot be done by giving water only. Sometimes I think the anhydremia which is often present in these cases is given too much attention. The skin seems dry, but this may not mean absence of water only. Nevertheless, I ordered 1 ounce of Ringer's solution given under the skin in each axillary space last night, and several ounces of water given by the mouth during the night. The baby passed urine twice in the last twelve

hours, which we must regard as conclusive proof that she is not suffering from dehydration.

To increase the blood volume I have been using lately the daily injection of human serum. This morning 6 ounces of blood was withdrawn from the median cephalic vein of the father by means of a large hollow needle. A small trocar and cannula is ideal for this purpose. The blood is received in a sterile tumbler, covered with several thicknesses of sterile gauze, and placed in the refrigerator.

You see the blood has clotted and fully an ounce of clear serum surrounds the clot. This will be aspirated into a large syringe and one ounce injected intramuscularly and subcutaneously into the baby. Tomorrow another injection will be given as more serum separates from the clot.

I give the baby in this way one ounce or more of serum daily for several days. By this means a great assistance is given to the food supply in filling up the blood-vessels and increasing the activity of the digestive organs.

Direct transfusion is a difficult operation in the atrophic baby. Then there is the task of typing the blood and finding a suitable donor. It is, moreover, doubtful whether a rapid filling of the baby's blood-vessels is as desirable as a gradual distention day by day.

We do not need corpuscles so much as albuminous substance, salts, etc., the normal soluble constituents of the blood. This is safely furnished slowly from the intermuscular spaces. We do not have to type the blood, and the simplicity of the procedure commends itself to the general practitioner.

We must look after the food supply. In an extreme case like this human milk is desirable. We have procured 8 ounces of milk from another mother, and the baby will be given 1 ounce every two hours. If this supply gives out, we will prescribe powdered protein milk, diluted 1 teaspoonful in an ounce of water to which is added 4 per cent. of milk-sugar. I prefer to give small quantities of food at first. The secretions are probably not sufficient to take care of a large amount at one time and vomiting is less likely to occur.



The baby will receive approximately 200 calories the first day, which is about 80 calories energy quotient. It must be remembered that the atrophic baby must have a relatively high caloric diet. Its ration should contain an energy quotient of 150 or more. Therefore, this amount of food must be increased tomorrow, when we will prescribe 2 ounces every three hours. Perhaps two days later we can increase this to  $2\frac{1}{2}$  to 3 ounces every three hours.

There is one curious phenomenon which presents itself in so many cases of extreme starvation during the reparation period. This is an acute diarrhea which may be fatal. It matters not what the initial cause of the inanition may be, as pyloric stenosis, cleft palate, improper feeding, or gastro-enteritis, a few days after the baby seems to be doing well and gaining in weight this diarrhea commences and often ends disastrously. It has been assumed that this diarrhea is due to overfeeding, that is, the threshold of tolerance has been overstepped, the food undergoes a rapid fermentation in the intestine, and the products of decomposition irritate the bowel and cause intestinal hyperperistalsis. My own studies indicate that the diarrhea is usually caused by a true enteritis, an inflammation of the intestinal mucous membrane. This is shown by the study of the stools in these cases. We have shown that the diarrhea is accompanied by a discharge of an enormous number of pus-cells in the stools. It matters not how carefully you feed the baby, this inflammatory reaction will occur in certain cases.

My own explanation is as follows: During the starvation period a large number of intestinal bacteria—colon bacilli(?)—penetrate the intestinal epithelium, but on account of the poor intestinal circulation the cells offer no resistance. As soon as the normal circulation has been somewhat restored, the resisting forces become active, an inflammatory reaction takes place, and the offending bacteria, dead cells, and bacterial products are extruded. This produces the diarrhea. In a few days the intestinal mucous membrane is cleansed, if the infant does not succumb, and thereafter the progress toward perfect recovery is rapid.



We expect this baby to get well, but it has still before it the stormy time of an enteritis in a few days. We hope that this will be mild in character.

**Subsequent Note.**—The infant received four injections of blood-serum. She commenced to gain on the third day; on the tenth day a slight diarrhea commenced and this continued almost continuously for two weeks. At first the stools were thin and watery and contained very few cells. Gradually they became thicker and an enormous number of leukocytes, lymphoid cells, and epithelial cells were found in the stool. A good maintenance ration of mother's milk and protein milk was continued. Gradually the cells became less numerous and the food was increased. The baby gained 2 pounds the first month and  $3\frac{1}{2}$  pounds the second month after the treatment was instituted.

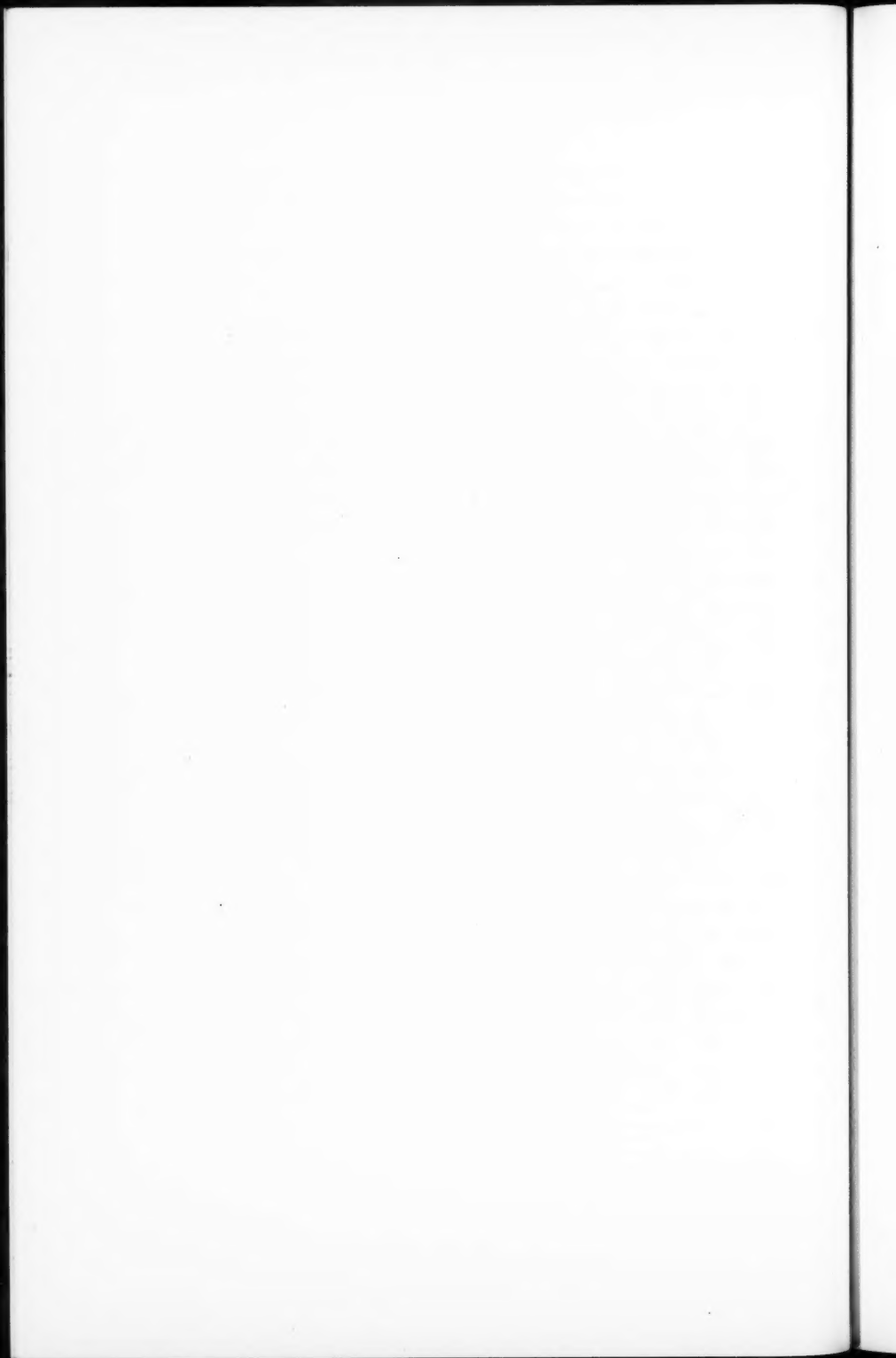
The baby will receive approximately 200 calories the first day, which is about 80 calories energy quotient. It must be remembered that the atrophic baby must have a relatively high caloric diet. Its ration should contain an energy quotient of 150 or more. Therefore, this amount of food must be increased tomorrow, when we will prescribe 2 ounces every three hours. Perhaps two days later we can increase this to  $2\frac{1}{2}$  to 3 ounces every three hours.

There is one curious phenomenon which presents itself in so many cases of extreme starvation during the reparation period. This is an acute diarrhea which may be fatal. It matters not what the initial cause of the inanition may be, as pyloric stenosis, cleft palate, improper feeding, or gastro-enteritis, a few days after the baby seems to be doing well and gaining in weight this diarrhea commences and often ends disastrously. It has been assumed that this diarrhea is due to overfeeding, that is, the threshold of tolerance has been overstepped, the food undergoes a rapid fermentation in the intestine, and the products of decomposition irritate the bowel and cause intestinal hyperperistalsis. My own studies indicate that the diarrhea is usually caused by a true enteritis, an inflammation of the intestinal mucous membrane. This is shown by the study of the stools in these cases. We have shown that the diarrhea is accompanied by a discharge of an enormous number of pus-cells in the stools. It matters not how carefully you feed the baby, this inflammatory reaction will occur in certain cases.

My own explanation is as follows: During the starvation period a large number of intestinal bacteria—colon bacilli(?)—penetrate the intestinal epithelium, but on account of the poor intestinal circulation the cells offer no resistance. As soon as the normal circulation has been somewhat restored, the resisting forces become active, an inflammatory reaction takes place, and the offending bacteria, dead cells, and bacterial products are extruded. This produces the diarrhea. In a few days the intestinal mucous membrane is cleansed, if the infant does not succumb, and thereafter the progress toward perfect recovery is rapid.

We expect this baby to get well, but it has still before it the stormy time of an enteritis in a few days. We hope that this will be mild in character.

**Subsequent Note.**—The infant received four injections of blood-serum. She commenced to gain on the third day; on the tenth day a slight diarrhea commenced and this continued almost continuously for two weeks. At first the stools were thin and watery and contained very few cells. Gradually they became thicker and an enormous number of leukocytes, lymphoid cells, and epithelial cells were found in the stool. A good maintenance ration of mother's milk and protein milk was continued. Gradually the cells became less numerous and the food was increased. The baby gained 2 pounds the first month and  $3\frac{1}{2}$  pounds the second month after the treatment was instituted.



## CLINIC OF DR. JULES M. BRADY

ST. ANN'S HOSPITAL

---

### INTRACRANIAL HEMORRHAGE IN THE NEWBORN

**Presentation of a Class of Four Children Aged Seven, Five, and Three Years, and Four Months Who Had Suffered This Accident. Puncture of Cisterna Magna When Lumbar Puncture is Without Result. Treatment by Spinal Puncture.**

THIS morning, gentlemen, I desire to discuss with you the subject of intracranial hemorrhage in the newborn. It is only in comparatively recent times that the profession has come to realize the frequency of this accident. In large maternities it has been determined that fully one-half of the still-born babies, and those dying shortly after birth, are the result of intracranial hemorrhage. When one considers the amount of pressure that the infant's head must be subjected to, it seems a great wonder that we do not have more of these kind of cases. There are those who believe that the hemorrhagic disease of the newborn is the responsible factor for the origin of this condition, but many obstetricians feel that the veins are torn as the bones of the fetal head overlap in the molding process.

Some infants manifest symptoms the minute they are born and are resuscitated only after the greatest amount of difficulty; pressure of the blood on the brain making breathing all but impossible. Then again a few days may elapse before the attendants are convinced that there is something wrong with the baby. It is of vital importance that a clear-cut picture be retained in your minds of the clinical picture, so that too much time may not be wasted before applying curative measures.

**Clinical Picture.**—The presence of blood in the cranial cavity causes symptoms from the side of the vagus, vasomotor, and

respiratory centers. The pulse is strong, full, and at times slow; later on it may become very rapid; the skin at times is of a peculiar white color (arterial constriction). In some of the babies there has been noticed a peculiar icteric hue of the skin which is believed to be due to the absorption of blood-pigments from the free blood. The respiration shows distinct changes, sometimes superficial and at times very rapid. Tonic and clonic contractions of the muscles of face and extremities direct our attention to the central nervous system. However, we do not always get such unequivocal signs, and it is easy enough for one not to suspect the condition until the advent of a spasticity of the muscles of an arm or leg at the seventh or eighth month, which gives us an explanation of what the trouble was during the early days of the baby's life. When we get the picture of stupor and often repeated convulsions, accompanied by a bulging fontanel and wide gaping sutures, I am sure that none of you would overlook the true condition. At this point I want to call your attention to a little practice which I carry out daily, and believe it will be of assistance to you when you are judging of the presence or absence of increased intracranial pressure. In all your newborns palpate the sutures frequently, especially the sagittal, so that you may be familiar with what is normal.

After we are pretty sure that the hemorrhage exists in the infant's skull we must endeavor to form an idea as to whether the blood is located infra- or supratentorially. The word "idea" and not "diagnosis" was used advisedly for the reason that such a thing as localizing the situation of these hemorrhages is out of the question.

However, if we early get the appearance of a bulging fontanel and have a cross baby that cries a great deal, sleeping but little, and refusing the breast, our first thought would be the presence of blood above the tentorium. If there is much of a hemorrhage at this site, death or permanent invalidism is going to be the lot of that infant. On the other hand, if you notice that the fontanel is slow in becoming distended, the infant is quiet and wants to sleep a great deal, is apathetic and early

shows a cyanosis, the probabilities are that you are dealing with an infratentorial hemorrhage, and a lumbar puncture or a puncture of the cisterna magna may cure the baby.

These 4 children I here show you were all expected to die as the result of an intracranial hemorrhage, but you see that they appear as well and hearty as one could expect. The mothers are perfectly satisfied with their progress.

The oldest boy, Charles, is now seven years old, he was first seen at the age of seven days here in St. Ann's Hospital. The presenting symptom was a severe icterus, which was of such intensity as to make one consider the possibility of an obstruction in the bile passages. Severe vomiting was also present, which was relieved by stomach lavage. Twenty-four hours later a profound stupor developed, the fontanel was bulging with wide separation of the sutures, and the respiration was very much embarrassed. There had been no convulsions and no muscular spasm. At birth the infant weighed 9 pounds and the obstetrician stated it had been a difficult forceps delivery. It was striking that in spite of the well-developed infant it would not cry and was very listless and apathetic. The icteric hue of the skin turned to a deathly pale color; the infant refused the breast and swallowing was difficult. The head appeared very much enlarged, globular in shape, with the frontal eminences very prominent. One was reminded very much of hydrocephalus. The baby's condition rapidly became desperate, and it appeared that it could live but a few hours. A fatal prognosis was given and an attempt was made to reconcile the mother by informing her that idiocy and paralyzed extremities would be in store for the infant if it were to survive. Lumbar puncture was performed and 60 c.c. of blood came gushing out; the fontanel receded, only to become distended again in a few hours. The respiration became better and the infant brightened up considerably. The following day lumbar puncture was repeated, with a free flow of blood from the needle; the third and fourth day this was repeated owing to the refilling of the anterior fontanel. In all, 240 c.c. were removed, but it was apparent that there was considerable admixture of cerebrospinal fluid in

the last 60 c.c. The anterior fontanel was still prominent, but owing to the marked improvement in the infant it was decided to stop the lumbar punctures. The tape-line revealed the circumference of the head to be 14.5 inches. It was necessary to nourish the infant artificially; it continued to thrive, and now, at the age of seven years, the mother reports that his work at school is entirely satisfactory. This child's recovery was a matter of the greatest wonderment to all who saw him.

The second boy you see here is almost five years of age; you see him walk and there is absolutely no evidence of spasticity of the muscles anywhere. He has an interesting history. When three days of age was first seen on account of vomiting, at the request of the mother, as she feared the baby might possibly have pyloric stenosis. At the first examination such a thing as intracranial hemorrhage was not dreamed of. The next day the baby caused quite a furor in the hospital by becoming blue and refusing to breathe. The prompt and efficient work of the nurses doubtless saved the baby's life. It was then observed that the baby did not swallow properly and that fluids regurgitated through his nose. It was impossible to feed him without causing choking spells. The true explanation of the cause of the symptoms was now suspected, and on lumbar puncture blood flowed from the needle. Symptoms from the side of the medulla continued for fourteen days, making it necessary to resort to tube feeding. If there are any signs or symptoms remaining by which one could tell that this lad has been through this accident no one has been able to discover same.

The third child you see here, this little girl, had violent convulsions shortly after birth. Relieving the intracranial pressure by making a lumbar puncture and withdrawing blood stopped the spasms and resulted in a perfect cure. Before we realized what could be accomplished by this simple operation of spinal puncture, attempts had been made to cure the condition by performing a craniotomy. We now know why this operation was so seldom successful. The hemorrhage takes place from more than one site, it is impossible to locate its seat, hence its removal is all but impossible. By spinal puncture we



can keep the intracranial pressure within the limits compatible with life. We know that the blood remains fluid in the skull for protracted periods and only a small amount undergoes coagulation. The liquid portion mixes with cerebrospinal fluid and is adequately taken care of by the organism. Without a doubt removal by spinal puncture of blood and cerebrospinal fluid promotes absorption of what remains. We do not presume for a minute that we remove all the hemorrhage through our needle, some must remain, but is adequately taken care of. However, we have not been entirely satisfied with our results following lumbar puncture. We have met with cases in which we were positive from the symptoms that we were dealing with a hemorrhage and still were confronted with a dry tap.

The babe which I show you here, four months old, was such a case. He was seen at thirteen days of age by us. According to the history twenty-four hours after birth, which was very difficult, convulsions appeared. An attempt was made to control them with chloral, which was only partly successful. Examination revealed a rather lifeless infant with icteric appearance of the skin which was very striking: the respiration was accompanied by a rattling noise in the throat apparently due to an accumulation of mucus. Swallowing was barely possible. The anterior fontanel was flush, but not bulging. There was a distinct separation of the margin of the sagittal suture. We all thought the infant moribund and expected its death in a few hours. Lumbar puncture was attempted twice, but was unsuccessful. The cisterna was then punctured and a large stream of black looking blood poured out of the needle. The infant was in such a desperate condition after 20 c.c. had escaped that the needle was withdrawn. The symptoms immediately improved and you see now the infant bids well to develop into a fine lusty child. Of course, it is too soon to pronounce as over all danger of Little's disease. We have to wait until the eighth month and then we are able to form a sound opinion.

This operation of cisterna magna introduced into clinical medicine by Dr. Ayer, of Boston, undoubtedly will enable us

to save many infants that heretofore were lost owing to the dry taps on lumbar puncture.

We will now repair to the dead house and I will demonstrate on the cadaver the technic of this operation. Drs. Porter and Carter, of San Francisco, in their book on Infants, give very clear and explicit directions which it would be difficult for me to improve on:

1. Place the patient in the lateral position as for lumbar puncture.
2. Take care to maintain the alignment of the head and the vertebral column in order that there may be no torsion of the spine.
3. Flex the head moderately.
4. Select a lumbar puncture needle of about 18 gage.
5. Place the thumb of the left hand on the spine of the axis.
6. Insert the needle at the midline just about the top of the thumb.
7. Force the needle upward and forward in the line of external auditory meatus and the glabella. Aim a little higher than the auditory meatus, and when the needle strikes the occiput, depress the point slightly.

Piercing the occipito-atlantoid ligament imparts a sensation to your fingers which makes you realize that you have entered the cisterna cerebellomedullaris. I must call your attention to the fact that you are passing a needle in close proximity to the medulla and extreme caution must be observed so as not to do any damage.

Sufficient punctures have been made to make us believe that while potentially a dangerous procedure, with care there need be no fear.

This little baby I showed you I believe is the first case of intracranial hemorrhage to have its life saved by this operation.

Dr. Ayer does not make mention in any of his writings of the possibility of curing intracranial hemorrhage in the newborn by this operation.

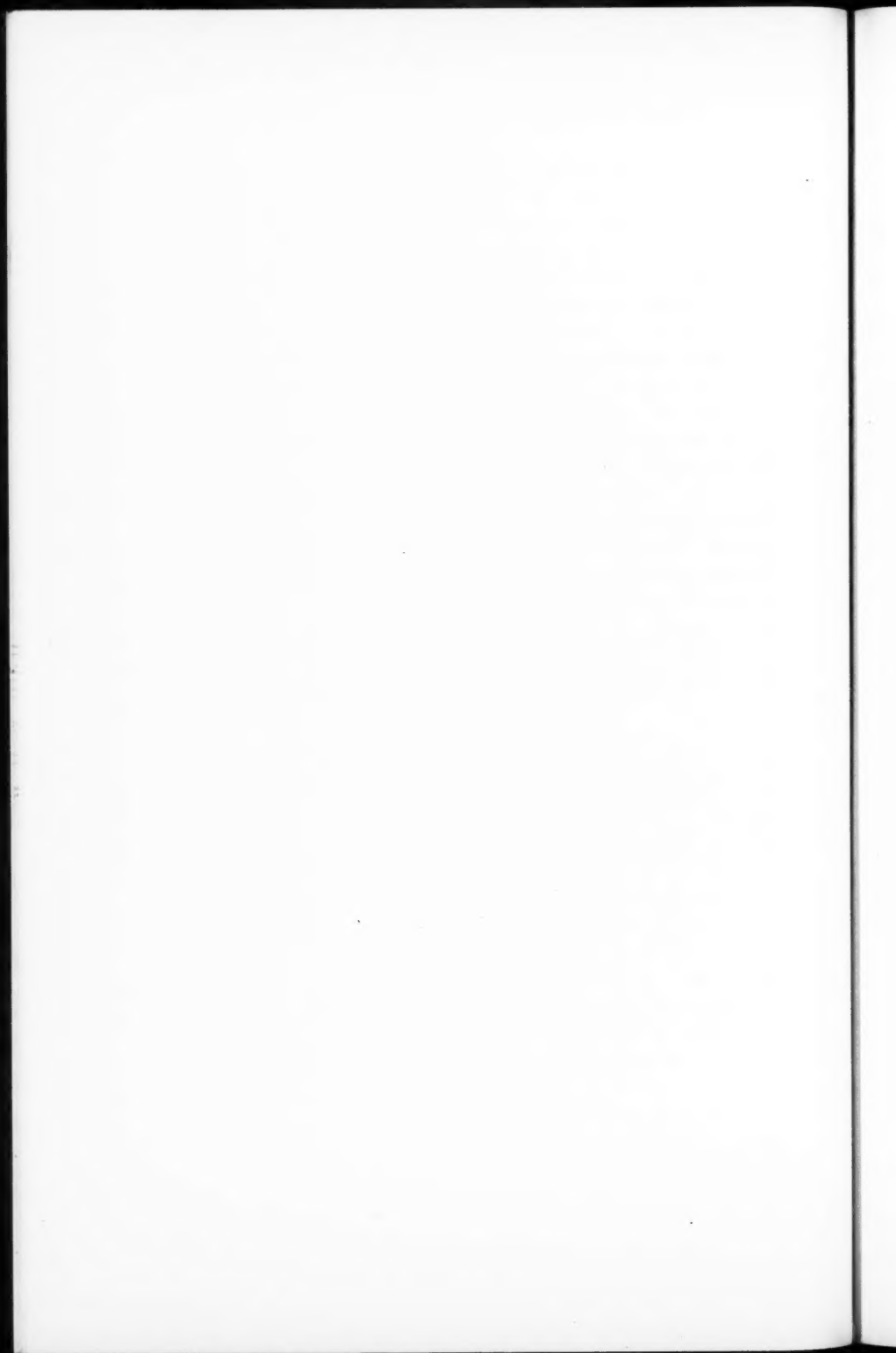
In another infant the cisterna puncture was resorted to after an unsuccessful attempt by the lumbar route a large:

amount of blood flowed through the needle. The life of the infant was not saved, however. At autopsy a huge hemorrhage was found covering one hemisphere and also some blood and clots were found under the tentorium.

STUDENT: Is it not advisable to inject blood to overcome the tendency to hemorrhage?

DR. BRADY: Yes, this point was overlooked, it is the routine procedure to give an intramuscular injection of blood derived from the father. This infant which was cured by cisterna puncture was not seen until thirteen days old, and as we know that the clotting time returns to normal by the tenth day, no blood injection was resorted to.

We have met with 22 cases of intracranial hemorrhage in which we have attempted to relieve by draining the subarachnoid space. Nine cases have made a perfect cure following lumbar puncture and one case gives promise of a perfect result by cisterna puncture.



## CLINIC OF DR. SIDNEY I. SCHWAB

BARNES HOSPITAL

### "HEART DISEASE" IN A NEUROLOGIC CLINIC

THE term "heart disease" is an extremely common non-professional diagnosis. It carries with it a great deal of dread and a certain degree of primitive terror, and often a very real and sharp sense of incompetency and inadequacy. The association between disordered action of the heart produced by emotion, often as not outside of the awareness of actual experience, and the idea that the heart is at fault is a very direct one. The evidence to the patient is conclusive, because he can feel and observe and otherwise test how his heart is beating and is conscious of sensations of an abnormal kind. If a more or less stereotyped set of abnormal symptoms relating to the heart becomes established as a routine reaction in no way associated with a logical set of causes, then the proof of heart disease appears established as far as the patient is concerned. The heart phenomena then become the presenting symptoms and the patient falls readily into the cardiac group in clinic distribution or in the choice of specialistic consultation. It seems worth while, therefore, to devote this clinic to a consideration of this group of cases, and an attempt will be made to demonstrate them from the neurologic point of view, rather emphasizing what is thought to be the mechanism of their production, than stressing the negative findings in regard to the cardiovascular apparatus. Only very brief histories are given and the facts in the case are presented as though they were readily obtained, when, as a matter of fact, the connection between symptoms and origins were only arrived at after very much effort and with the expenditure of time and patience. It must be understood too that in some of these cases the true explanation may lie quite

apart from the story as given, but the effort to find some kind of connection between causes and symptoms was felt to be successful, from the point of view of therapy, if a direct and logical sequence could be established. Something to "work upon" was thought to be more important than a long-drawn-out analysis, Freudian or otherwise.

There has been selected then for this clinic a group of cases presenting symptoms which pertain to the cardiovascular system. Such patients are as a rule sent to the cardiac clinic of the dispensary or assigned to the medical service in the wards of the hospital. Physical examination shows the heart and vascular system to be normal and in other respects there are negative findings. They are, as a rule, then transferred to the neurologic service with the diagnosis of nervousness, functional heart, hypochondriasis, neurasthenia, etc. A certain percentage of such cases is found to be the subject of various abnormal psychic conditions, best described under the term "conflict." Others show nothing of this kind and remain a puzzle to the internists and neurologists until such a time as their symptoms disappear or something happens to the cardiovascular system which gives a substantial basis for the origin of both findings and symptoms. During the war such cases were frequently grouped in a rather haphazard way under the term "effort syndrome." This term should be given up at the present time, as it is of no particular value in either delimiting this group or clarifying the symptoms which are found. The interest and importance of this class of cases aside from the nature of the problem itself is found in the severe handicap with which it is burdened and the incapacity which the cardiac sensations produce. The explanation of these curious conditions is by no means certain, and the assumption that there is no organic change in the cardiovascular mechanism is by no means assured. Yet the importance of the psychic point of view emphasizes the necessity of attempting to evaluate that phase to see if some light cannot be thrown on these obscure cases. The necessity of attempting to formulate some kind of theory or notion is apparent, and a very general statement of a point

of view may well be given before the individual instances are presented for consideration.

This notion may be stated very briefly as follows: One of the most common causes for the acceleration of the heart beat are experiences strongly tinged with emotion. The emotion most commonly aroused is fear. The fear formula consists of tachycardia, increase in respiratory rate, sweating, sensations of binding, constricting, or of an oppressive kind in and about the chest, and often, indeed, a distinct sensation of pain over, about, or in the heart. Various emotions other than fear can produce phenomena of a similar kind. Certain other secondary reactions are common and they are often seen as residuals of an acute fear experience. Tremor, vertigo, decrease in muscle tone, loss of reflex inhibition, a sense of physical weakness, or mental perturbation and confusion. It is seen from this general description that the cardiovascular apparatus is chiefly concerned as far as the objective and subjective phenomena are manifest. Out of these separate items a fairly accurate clinical picture of the so-called cardiac neurosis may be built up. Such reactions can be called forth in three other related conditions other than actual experience: in anticipatory experiences associated with emotion, in retrospective experiences of a like nature, and in experiences the nature and kind of which are unknown and beyond the field of awareness of the individual. This leaves then a broad field for investigation in cases which by the most careful methods of clinical study the essential integrity of the cardiovascular mechanism has been determined.

It is necessary now to mention a further essential in the establishment of the cardiac problem; that is, the tendency toward the continuation of the phenomenon in the absence of the emotional stimulus. This habituation or pattern retention constitutes one of the most important phases of the problem so far outlined.

The physiologic theory may then be summarized in this fashion: (1) Emotional experiences, chiefly of fear, are capable of producing a picture of acute heart distress. (2) Anticipation, memory, and their unconscious play may produce a like

picture. (3) By habituation a common pathway of retention may be established which lowers the inhibitory threshold in such a way that minor or associative stimuli may establish the totality of the trend of symptoms. (4) The reaction readily becomes conditioned, set and crystallized by previous experiences. (5) The association of all these symptoms or some of them as a current reaction of which the patient is supremely aware constitutes for him a picture of heart disease which has the necessary conviction of reality, and serves as an emotional intensifier.

**Case I.**—The first patient to be presented is one who has been under observation off and on for a period of nine years. She is now twenty-four years old, married about five years, and has one child. You see a small well-developed, apparently healthy young woman with a somewhat anxious expression. Her pulse-rate in the presence of a medical audience is about 124. At rest and quiet in her room her pulse-rate becomes very close to the normal. On admission her chief complaint was pain about her heart with shoulder and left arm radiation and a sense of constriction about the chest, difficulty in breathing, and attacks in which fear of death and a feeling of dissolution are present. She also complains of a pulsing or throbbing sensation in her chest and is annoyed by constantly hearing her own heart beats. These symptoms often become so pronounced that she is compelled to go to bed for days at a time. A brief outline of her history is as follows: In 1909 after a dose of diphtheria antitoxin she had what was evidently a pretty severe serum reaction. She made what was apparently a complete recovery. A number of months afterward she noticed that slight emotional stress often trivial in character would make her heart beat rapidly and cause her to breathe with difficulty. For one reason or another at that time she associated these phenomena with fear of dying, and the fear of sudden death was one of the most constant features of these attacks, both preceding them and occurring during them. She came under my care with the chief complaint of tachycardia and fear of death. A number



of such attacks were observed and the following were noted: There was always present a tachycardia, polypnoic type of breathing, no cyanosis, some sweating, and an anxious terrified expression on her face. She was often in a state of abject fear and terror, believing that she was dying. Assurance that she was not going to die was generally sufficient to stop the symptoms and after a while she would regain her self-control, although the tachycardia persisted for many days or weeks. Afterward she was enabled to go about her duties and seemed perfectly well. From time to time during these early years she was seen by other physicians, and they, as a rule, appreciated the emotional character of her symptoms and she was treated accordingly. Some time between 1917-19, shortly after she was married, she was told that she had a leak in her heart and that this was due to chronic appendicitis which had produced a vegetation on the valve. Furthermore, she was informed that the only way she could be saved was to have her appendix removed. She was also advised to avoid pregnancy, because she was physically unable to give birth and take care of a child. This was in brief her story when I saw her again after a period of two years. She had now formulated a complete picture of cardiac disease, to which she reacted in a perfectly logical manner. Emotional distress, disappointment, worry, fright of anything that happened of an unusual nature, would start the train of symptoms going, and with the conviction that she had a heart that was leaking would carry out to the last detail all that was associated with the term "heart disease." To be noted too as an added factor in fear production was the avoidance of pregnancy which was carried out by coitus interruptus. A complete restudy of her case was undertaken. Gastro-intestinal study showed no abnormality and no signs of appendicitis, the general physical was completely negative, cardiographic and x-ray pictures of the chest were entirely without result, there was no thyroid enlargement, and metabolism rate was normal. She was sent to a specialist in heart disease and also to various others in order to determine if there was the slightest possible physical basis for her symptoms. All of them returned negative

reports, and she was persuaded again and again of the functional character of her symptoms. There remained then the almost constant tachycardia, the attacks that have been described of fear and premonition of sudden death, all in the presence of perfectly normal physical findings. With this established she was advised to become pregnant. After the birth of her child many of her symptoms disappeared and nothing was heard of the patient until some three years after the child was born, when she came under observation again with a repetition of the former symptoms, but in a more exaggerated form. The attacks would come on under all possible circumstances, but chiefly in the presence of her husband, toward whom she was apparently developing a marked antipathy, particularly in the matter of physical contact. She complained especially of cardiac pain with shoulder and arm radiation, a feeling of oppression about her heart and chest, difficulty in breathing, and an alarming sensation of impending death. During such attacks the pulse-rate was about 120, 130, and 140. Breathing was shallow and rapid, pallor, some sweating, but no cyanosis. The emotional origin of these attacks seemed certain, so the patient was put into as receptive a state as possible with the intention of an analytic study for the purpose of finding out if possible some source of conflict process not apparent from superficial questioning. After a good deal of effort and a great deal of time and against a great deal of opposition she finally admitted that she had fallen in love with a friend of her husband's and that some kind of extramarital relations had been going on for at least two years. This combined with the growing indifference to her husband, the growth of the antipathy referred to, the discontinuance of sexual relationship produced the conflict. It was a completely conscious one consisting of the opposing tendencies in the patient's mind, the love for the other man, and her sense of duty and obligation to her husband and child, both of whom she was fond of. She confessed to a great respect for her husband and an intense devotion to her child. She would not face the solution of her conflict by divorce or confession to her husband and so she remained caught in the meshes

of the impasse created by a situation from which no way of escape seemed open. The emotional reaction escaped by following the old established pattern, long ago laid down through the cardiac pathway, and her release from the impending conflict pressure was through the cardiac attacks which have been described. You see this patient now in a comparatively free period. Her more violent seizures have almost disappeared and with a complete knowledge of their cause and mechanism she has already reached a state of comparative freedom from them.

The point of this demonstration lies simply in the fact that emotion, no matter by what circumstances it is aroused, can produce evidence of cardiac disease, when this pathway or pattern has been laid down by repeated experiences. Associated phenomena are attached as other factors become added until a stage is reached where almost any emotion finds its way of escape not in a physiologic way through muscular reaction, but is side-tracked through the cardiovascular pathway. The therapeutic power of understanding and facing the situation frankly and courageously may supply something of the normal inhibitory influence which in this patient's case has so nearly vanished.

**Case II.**—The second case presents an entirely different problem, belonging to the group in which there is eventually found some definite condition of the cardiovascular system which furnishes a partial explanation at least for the heart symptoms, even then the psychic disturbances are so far in excess of the anatomic causes that a diagnosis of anxiety neurosis was concurred in by the heart specialist in consultation in the wards of the Barnes Hospital. It is interesting to note that at some period during the time the patient first came under observation from 1916 to 1923 a high degree of hypertension together with an enlarged and hypertrophic heart developed. As there was no history of acute infectious disease in this interval, other than a sharp attack of influenza, the cause of the hypertension remains a mystery. You see a robust looking man of fifty, he has an anxious expression and seems a bit apprehensive, his color is good, but rather "damp," there is some cyanosis about

his lips, and a slight but definite tremor of the tongue and at the corners of the mouth, he is restless and obviously more ill at ease than the circumstances of his surroundings warrant. He enters the neurologic service now with the chief complaint of anxiety and tachycardia. He was first seen in 1916 when he was forty-three years of age, he had 4 children and had been married then about eighteen years. He is a storekeeper and owner of a store in a small town in Illinois. His chief complaint when first seen had to do with dreams or nightmares and states of cardiac stress afterward. He would suddenly be aroused at night with sensations of great anxiety and fear. He became acutely aware of a rapid beating of the heart and some difficulty in breathing. He described also a feeling of faintness, sweating, and great terror. It was impossible to associate the content of his dreams with the phenomena that have been described. Very often they were not terrifying and as far as he could remember they did not have to do with terrifying events. He was sure that these nocturnal experiences followed any unusual emotion during the day, particularly if he had had something to worry him in his business. As a result of these experiences he began to feel a diminished confidence in himself and was aware of a definite feeling of inadequacy and a loss of effectiveness in business. A marked degree of cardiac suggestibility developed so that any reference to heart disease awakened a definite train of symptoms which become a kind of stereotyped reaction. He was continually counting his pulse, and he noted that after eating, for example, his pulse would always be more rapid than at other times and that often during the day he would be conscious of an attack of anxiety with rapid heart beat. In this period physical and neurologic examinations were negative. The only abnormal finding was the tachycardia, which was particularly pronounced during examinations. The mere fact of undressing and preparing for heart examination would send his pulse-rate up fifteen or twenty beats. The experiment was often tried of preparing him for an examination, taking his pulse, and then letting him lie quietly for a half-hour. The drop in pulse-rate was quite remarkable.

His family physician frightened him a great deal by calling his attention to the fact that his heart beat was rapid. During the year of 1916 he was seen at monthly intervals, and with assurance that his heart was in good condition and with directions for more hygienic ways of living and eating he was enabled to get along with very few attacks. He put on weight and became so much improved that he was practically without medication during most of the time until he presented himself again in April, 1923. He had much the same complaint, but, in addition, headache and vertigo. He was particularly concerned with the sensation of anxiety and fear of death and a conviction that something was going to happen to him. There was a great deal of business worry at this time and he began to have the nocturnal attacks that have been described. He had been free or almost free from these for a number of years. At this examination in April, 1923 for the first time the heart was found to be definitely affected. He had rapid pulse, often reaching 120, and on occasions 140, a systolic bruit in the second interspace, left not transmitted, apex-beat in the sixth interspace and a marked accentuation of both second sounds. The heart was slightly enlarged and the apex-beat loud and booming. The most surprising finding, however, was the high blood-pressure 220 over 90. He was very much disturbed at this examination and became slightly cyanotic, sweaty, but not dyspneic. The systolic pressure was taken at intervals of one-half hour with complete rest during these periods, but it never varied but within slight limits. He was then sent to the Barnes Hospital for more complete study, and you see him now after various examinations have been completed. He was made a special problem for cardiac investigation. The physical findings outside of the heart were practically normal. The urine showed a slight trace of albumin and occasionally a fine granular cast. His N. P. N. was 38.5. Cardiograph showed a slight left ventricular preponderance. Wassermann was negative. There is a slight cardiac enlargement and a widened arch of the aorta, confirmed by 7-foot plate. The aortic second is plus, over the pulmonic second, there is a rough systolic murmur found at the

second intracostal space, right, but not transmitted. The sound is good in quality, pulse 84, blood-pressure 196/106 and 210/110. The arteries are barely palpable. The only evidence of arteriosclerosis is found in the hypertension. The note made by the cardiac consultant is as follows: "The type and duration of symptoms with previous negative findings and symptomatology would fit this case into the group of anxiety neurosis of the cardiac type. Present symptoms do not seem to be dependent upon hypertension." The diagnosis made on the hospital record is anxiety neurosis and hypertension. There is present in this case then a combination of marked psychic reactions and a slow and gradually developing hypertension with some changes in the heart which would correspond with high systolic pressure. The most noticeable and striking feature of the case is the presence of a high degree of tachycardia following the slightest emotional stimulus or indeed following anything that calls the patient's attention to his heart. When he was in the ward lying quietly in bed the nurse often found his pulse-rate comparatively low. As soon as a physician approached or a diagnostic maneuver carried out in reference to his heart the effect upon his pulse-rate was definite. In all of these experiences associated with the fixed idea concerning his heart evidences of anxiety, fear, and apprehension were pronounced. His condition often seemed to approach that of anginoid attacks. He never complained of pain or sensations of pressure in or about his heart as were described in the preceding case. In a careful study and analysis of this man's personal history, his social, domestic, and business relations, nothing in the way of a conflict was found. He was a man much given to worry about his business, but not more so than would seem justified by the facts themselves. There is present then in this case a mechanism of fear reaction which finds its symptomatic expression in the cardiovascular system. This is to some extent damaged or at least presents a type of low threshold response which creates a group of annoying and disturbing symptoms of which the patient is cognizant. The strain of these emotional reactions produce a greater effect in this case because the physical apparatus

through which the emotion is given expression is less resistant and is much less efficient than would be in a case of a normal person. Apparently, therefore, the outlook for such a case is distinctly more dubious than would be the outlook in a case in which the cardiovascular mechanism is intact. An interesting question as to the causation of the hypertension presents itself. Is it possible that a fairly normal cardiovascular mechanism which has to submit for a number of years to repeated storms of emotional side-tracking, responds by a form of overuse causing a degree of hypertension not justified by the feel of the peripheral vessels, and can the heart slowly hypertrophy in consequence?

Neither the presentation of this case nor the description given can begin to give the actual distress under which this man is living. He is almost constantly aware of his heart and pulse-rate, and he is continually haunted with the idea of incapacity, failure, and death. The emotional stream associated with these and similar ideas is in a state of almost continuous activity.

**Case III.**—The third case is a man of thirty-seven years of age, a tailor, who comes into the hospital with a complaint of pain in the chest and right shoulder and with a history of attacks in which he becomes pale and tremulous, is conscious of a violent beating of the heart, and is anxious and tearful. The attack is followed by a state of exhaustion in which the patient is compelled to rest. You see here a man of ordinary appearance, apparently in good health, rather stolid and unimaginative as far as expression is concerned, well built and strong. He sits quietly and does not seem to be worried or anxious. He gives the impression of a man without much emotional instability and without a neurotic trait. The origin of these attacks is as follows: About one year ago when asleep he dreamed that his first wife touched him and told him to come along with her. His immediate reaction was an attack such as has been described. Following this dream he had "spells" of a like kind whenever he thought of his first wife and often when he



did not. He had frequent attacks of this sort each day. The attacks have been such a surprise and are so unusual an experience with him that he is very much puzzled as to just what they mean. He believes that he is seriously ill and that his symptoms are due to some affection of the heart. Inquiry into the past history of this patient shows very little that can be brought into relationship with the present illness. He has had no serious infectious disease, has led a normal life in every way, has had no bad habits, and up to the time of his present illness considered himself perfectly well. The most important etiologic factor in the past history is not that of disease, but has to do with his social and domestic life. His first wife died as a result of cardiac decompensation in 1913 after a protracted illness of two or three years' duration. He was very devoted to this first wife and took care of her during her illness as much as he was able to do and at the same time attend to his business. Four months after the death of his wife he married again, much to the surprise of his friends and much against the tradition and custom of the circle in which he lived. In his second marriage he found as much happiness as he did in his first and has shown the same devotion to his second wife as he did to his former wife. However, during the whole period up to the time of the outbreak of his present symptoms he was in a state of constant concern over the fact that he had married so soon after his first wife's death. The greater his happiness in the second marriage seemed to be, the more critical was his attitude in regard to his conduct defect in so soon forgetting his first wife. In order to distract his attention from this ever-present conflict he tried to divert himself in various ways. He was a frequent visitor to the movies and other places of amusement and was eager to take part in social pleasures. After a number of years he succeeded, as he put it, in forgetting his first marriage. The sources of self-criticism and accusation gradually lessened and he was comfortable and contented until the dream episode, which occurred about a year ago. Now when he thinks of or imagines that he sees his first wife—a condition which has developed in a marked fashion since this dream experience—he is aware of a



pain across his chest and is conscious of rapid heart beats, difficulty in breathing, dizziness, and sweating. At such times he becomes very pale. He was sent to the Barnes Hospital in order to exclude or include a definite cardiac condition which might account in some way for the symptoms which have been described. Examination, however, reveals a normal cardiovascular apparatus with normal function in every way. His blood-pressure is 145/80, heart sounds are regular, there are no murmurs, the second sounds are equal, and not exaggerated. The neurologic examination is negative except for an absence of smell, which followed some nasal operation. The lumbar puncture shows only four cells, normal curve, with a negative Wassermann. Urine and blood are normal and there is a normal cardiogram. Here then is a case in which the cardiovascular as well as the general system appears to be perfectly normal and perfectly adequate in every way to take care of the normal variations in the day's activities. The symptoms for which he seeks medical advice have to do with emotional responses shown by increased pulse-rate, palpitation, vasomotor reaction, and a sensation of pain in the chest. A case of this kind would scarcely ever be mistaken for heart disease after the ordinary study of the cardiovascular system was carried out, but the individual himself associates symptoms of this kind with disease of the heart and is responsive to that fixed idea. It is important to appreciate the mechanism by which the emotional effect is brought out and how it displays itself. If you will remember the history, you will note that up to a year or so ago this man was conscious of a conflict in regard to his ideas of right and duty in respect to a marriage so soon after the death of his first wife. When he was clearly aware of the psychic conflict he attempted to retreat, so to speak, from its effect by what he called diverting his mind. This was brought about by various social activities of one kind or another, going to the movie picture shows, theaters, and things of that kind, and probably by more active processes of repression and no doubt also by the natural tendency to forget. After a while he found that it was not necessary to do this. In other words,

he was able to suppress the conflict and divorce it from his every-day experience and from his every-day memory. The conflict then may be said to have been dormant and buried in consciousness. It was aroused to its full force again after the accidental occurrence of a dream which brought to conscious realization in a vivid way the old source of self-criticism and self-accusation. Now he may be said to be suffering from the emotional residual of this conflict, the nature and importance of which he had almost forgotten. The therapeutic plan followed in this case was that of assurance based upon as clear an understanding of the nature of a fear reaction as was possible in a man of his grade of intelligence. Efforts were made in this case to show the nature of fear and the response in respect to symptoms produced by them, and to convince him that these attacks were of purely mental origin and could be accounted for by the memories and recollections which were brought up in his mind by the dream which has been described. It was further demonstrated that the attacks themselves were not dangerous and were not necessarily incapacitating, and that they could be overcome by frankly understanding what they were about and how they happened to occur. He was told also that the best way to counteract them was to have as clear-cut a knowledge of their origin as possible and to keep the source of conflict as clearly in his mind as possible, and to try to make adjustment through a more emphatic interest in his present problems and his present every-day life. During the last few days of his stay in the hospital the attacks have ceased. Patient was seen once again after leaving the hospital and he reported that the attacks had grown progressively less and he felt that he was able now to control them.

**Case IV.**—For three years this patient, a man of fifty-four years of age, has had numerous attacks the nature of which has been a puzzle to various physicians who have examined him. These attacks occur chiefly during sleep. The patient suddenly awakens with a start and with the sensation of his heart turning over. This is accompanied by a feeling of impending death and

indefinite pain in the chest. The patient is a spare, middle-aged man with a rather fixed and mask-like expression. This, however, is a personal characteristic. Up to three years ago the patient had been a very busy, active, and energetic business man. He has had charge of and owned a private rural telephone station which he started and developed into a considerable plant. He had become a kind of expert in rural telephone business and his advice was often sought in matters connected with the problems of rural telephone communication. During his activity in this business he was an up-standing man of affairs in his community and accumulated considerable wealth, was diligent, industrious, and enthusiastic. He always worked hard, but was much given to worry over the details of his business. His past history shows nothing of importance in regard to his present condition. There is a history of malarial attacks and also of attacks that were thought to be articular rheumatism, at least, during the last one of these in 1919 he was treated at Hot Springs with baths. There is no more accurate information concerning these illnesses. Following the first attack of rheumatism he seemed to have made only a partial recovery, at least he felt that he was not as vigorous as he was before. Some time in 1919 he began to notice that he was less able to carry on his business than he was before and noted also that he had difficulty in sleeping. This was called nervousness by his physician and after a time he was advised to sell out his business and stop work. This he did in January, 1923. On January 15, 1923 he was mixed up in a rather complicated transaction having to do with some telephone business and he was very much disappointed at the outcome and suffered some financial loss. This apparently worried him a great deal and he felt that his judgment, energy, and initiative had not been equal to the emergency. On February 20th he had an attack of weakness with sinking sensation, which was the first manifestation of his present condition. It was during this attack that he first noticed a sensation as if his heart were turning over. As soon as he perceived this he became somewhat confused and excited and jumped out of bed and walked rapidly up and down the

room. There was some question in his own mind as to whether he quite knew what he was doing, but evidently there was no loss of consciousness at this or any other attack. An attack observed at the hospital is about as follows: Patient asleep at night and some slight sound appears to disturb him, he immediately wakes up with the sensation that his heart has stopped. Then there follows a period of slight confusion, anxiousness, and excitement, and he jumps from his bed and walks rapidly up and down, and on one occasion out into the corridor. While there is no acute anginal pain, there is a considerable sense of pressure and discomfort over the chest. After the muscular exertion of jumping out of bed and walking his heart appears to start again, and he feels fairly well with the exception of a marked degree of weakness and anxiety. Owing to the age of this patient and the questionable character of the attack, especially from the standpoint of confusion and possible loss of consciousness, a careful study of the patient's cardiovascular system was undertaken in order to be able to exclude angina pectoris. The heart was not enlarged either to percussion or to x-ray examination. The rhythm was regular, rate about 80, sounds of good quality. Exercise test did not increase heart rate above that found in the normal. Blood-pressure was low—100/68—cardiograph was normal, and all other physical and laboratory findings were found to be negative and the neurologic examination showed nothing out of the way. The note on cardiac consultation is as follows: "Symptoms in this case do not seem to be of a cardiac nature. The attacks of sudden palpitation suggest the possibility of paroxysmal tachycardia. The attacks themselves might cause the sudden fear and produce a sensation of suddenly startling the patient." The only marked finding is a moderate degree of hypotension. The diagnostic conclusion was an anxiety neurosis of cardiac type. This case belongs to a group in which there is no apparent psychic conflict and no direct psychic cause that can be determined by a study of the patient or his past history or his present psychic condition. The only etiologic important factor in the past history is the period of intense worry and concern over his personal

affairs, his giving up his business, and the period since then of idleness. The acute business emergency which he passed through during the month of January of this year would seem to have been the direct cause of the development of his insomnia and of his anxiety. Yet, there appears to be nothing in an experience of this kind other than the mental fatigue that it produced which bears any direct relationship to the attacks complained of. The significance of the hypotension must not be lost sight of, as this is distinctly abnormal in a man of this age. Here again, as in a former case, the cardiovascular apparatus is not altogether normal, is a less efficient mechanism, and bears for this reason the strain of emotional reaction less well. Just how to interpret the sensation of the heart turning over is beyond our knowledge at the present time. This is not an uncommon way of describing a feeling associated with what appears to be some abnormal movement of the heart. The intense emotional reaction which results is the curious feature of this case. The impulse to move about and obtain some sort of emotional release by walking rapidly is an unusual feature, even in acute functional heart attacks. Patient explains his activities by asserting that such movements start his heart beating again. He is thoroughly convinced that during the attacks his heart actually stops. It would be interesting if this could be used as a diagnostic test for the functional character of such an attack, as automatic rest is the usual physiologic formula of protection in acute heart distress, caused by actual lesional effects in the heart muscle or in the heart innervation.

**Case V.**—The last case is concerned with a purely emotional reaction in a young girl of sixteen years of age. A series of emotional experiences produced first a series of reactions in the cardiovascular system and out of that has arisen so great a fear that she finds it impossible to leave the house, and for almost three years has had to be accompanied by somebody whenever she went out. In addition to the fear of death, associated with the cardiovascular symptoms, she is also afraid of fainting and losing consciousness. The immediate history of this condition

has reference to an experience in a moving picture show, when the patient saw the presentation of a drama in which the chief item seems to have been the electrocuting or the preparation for the electrocuting of the chief villain of the play. When this gruesome attempt at realism was presented on the screen she had an attack of tachycardia, with a sense of constriction around the neck and throat, and intense palpitation. She was taken from the theater to her home and was in a condition of marked emotional excitement and nervous shock which resulted in the continuance of fear reactions in respect to pulse, palpitation, etc.

This patient is now sixteen years old and the occurrence took place when she was about thirteen. She is a somewhat apathetic and apprehensive looking girl, about normal weight, rather red lips, but otherwise somewhat pale. Patient gives a very clear account of her condition and with little tendency to exaggerate symptoms. Following the experience in the moving picture theater she developed a striking state of suggestibility, so that any untoward occurrence, especially if it had to do with sickness or disease, made a deep impression upon her and caused a repetition of the fear formula present at the original onset. For example, in some of her attacks she feels a sudden stiffness of the right arm and leg and becomes worried because she thinks she might be paralyzed. This has reference to a case of hemiplegia occurring in a relative of hers. She has also a fear of falling down. This is attached to an experience in which she saw a child fall down in a fit. She is fearful in a crowd. If there are many people about she begins to feel flushed and uncomfortable, becomes aware of the sensation in her chest, constriction around her throat, and feels the beating of her heart. Patient shows a rather minor development of the general muscular system, but the muscles feel firm, however, and there is no apparent loss of strength. The pulse at this examination is slightly increased, but not more so than is usually seen in a patient under examination or when patient is demonstrated in a clinic. There are no general physical findings and no positive neurologic findings of any sort. The heart is of normal size, first sound clear and distinct, there are no accentuations

of second sound, no adventitious sounds are heard, blood-pressure is normal, and the cardiovascular system in a state of rest seems to function perfectly well. From time to time, in addition to other symptoms, patient complains of very severe pain over the left breast and along the rib margins. These attacks of pain are associated with the emotional attacks here described.

This patient was first seen on March 16, 1921, and at intervals up to the present time. On December 12, 1922, she complained of a severe pain over her heart and this pain was felt instantly when she heard or read that anybody was sick or about to die. The patient keeps away from school and remains at home, seldom leaving the house unless accompanied by some one, generally larger or older than herself. Her dreams have to do largely with emotional experiences of one sort or another. She has constantly recurring dreams that she is about to die. As this patient was observed during the course of the year following her first examination it could be seen how the whole symptom complex associated with her fear became more and more stereotyped and crystallized, so that the sequence of symptoms became very exact and followed a set formula. The pain which was at first comparatively insignificant has now become a very definite part of the whole reaction, which now consists of a sense of fear, anxiety, constriction about the chest, difficulty in breathing, palpitation, a sense of rapid beating of the heart, and a very definite acute pain which is localized with great exactness over the heart area. During the worst of these attacks she becomes quite faint and dizzy and has a very distinct fear of falling. The relation of this symptomatology to her initial fear experience seems quite clear and the accumulation of other experiences of an emotional nature has accentuated the severity and acuteness of the fear reaction.

As far as could be learned investigation of the previous history of this patient has shown nothing similar and, while she has always been of a neurotic type and comes from a family of a similar sort, there is nothing to suggest any abnormal emotional tendencies. It is quite possible, however, that the whole recent association of fear with cardiovascular symptoms may have



been due to early childhood and infantile experiences. It was thought best, however, in such a case to limit the investigation to the acute onset and see if it were not possible to train this patient to establish a kind of artificial inhibition over these attacks. So far it has not been possible to accomplish this.

This then is an example of anxiety neurosis with emotional outlet through the cardiovascular system presenting the symptoms commonly associated with the term "heart disease." All that is necessary to establish the veritable picture of this condition is to blot out of actual awareness the original incident, to repress the actual experience or to replace it by something trivial or accidental, or for the patient to refuse to admit that such an incident ever took place. This mechanism is mentioned because in such cases as this it is quite possible that the movie picture etiology, for example, may not be the true one, but something vastly more laden with emotion and conflicting motives. In such instances the attempt at uncovering needs a more complicated type of analysis than was made use of in this case. There remains then the picture of acute heart distress as the presenting symptom and for that reason this case falls within the category of the title of this clinic.

The cases shown in this clinic are not unusual. They are among the commonplaces of hospital and private practice experiences. They point to the fact that symptoms associated with heart disease often mask emotional reactions depending upon conflicts of a social, domestic, and economic kind. Their successful treatment depends upon the ability, understanding, and intelligence of the physician to appreciate conditions such as these and to attempt to see beneath the presenting symptoms the play of emotion and the currents of feeling which often cause symptoms such as have been described. The most careful and scrupulous methods of examination and study should be pursued in order to be certain that there is not a physical basis underlying the symptoms displayed. Treatment must be directed toward the understanding and, if possible, the solution of the conflict. Where the latter is not possible, as is often the case, a clear presentation of the various factors producing the conflict frequently proves of positive therapeutic benefit.



## CLINIC OF DR. FRANCIS M. BARNES, JR.

FROM THE NEUROPSYCHIATRIC DIVISION, ST. MARY'S HOSPITAL

### HYSTERIA

IN presenting these few patients to you this morning it is appreciated that we enter upon the consideration of a group of mental disorders in reference to which there have been held in the years past and in the present time the most divergent conceptions relative to nosology, etiology, and symptomatology. Some of these patients have been presented to this class on a previous occasion. They are now brought before you again to demonstrate, by the changes which have occurred in the meanwhile, how very important it is that the patient be studied in the entire course of the disease and not alone at one particular period of this course in cross-section-wise manner. This is most important from the viewpoint of diagnosis and, also, because it illustrates so well and distinctly how the superficial clinical manifestations of one mental disorder may simulate those of another essentially different group. Before showing any patients a few general remarks will be made concerning this group as a whole.

It is by some questioned that the group to which we are to give our attention this morning are properly included among the mental disorders, the argument being that they are not truly psychoses, but represent another class of nervous system dysfunctions known as neural. Two of the patients whom we will later present for demonstration will illustrate only too clearly how indistinct this dividing line between the neuroses and the psychoses may become at times. Perhaps the euphemistic tendency which endeavors to prevent "pronouncing" an individual insane because of the stigma of disgrace carried with such a condition has in part helped in the attempts made to

separate the consideration of the insanities from all other disorders of the nervous system, peripheral or central. Then, too, there is a sociolegal side to those mental disorders which produce conduct disorders defined by the statutes as results of unsoundness of mind which furthers this attempt at separation. Similar statutory regulations for the group which we have under reference are seldom called upon because of the mental disorder, but, nevertheless, these diseases none the less by their symptomatology betray their basis in such mental abnormality.

Whether or not hysteria, to which psychoneurosis we shall devote our particular attention on this occasion, should be more properly classed as a psychosis is a moot question, largely of academic importance. However, you may justly ask if there is any feature by which the psychoses may be differentiated from the neuroses. Upon an anatomic organic basis such is impossible. With certain of the psychoses an organic basis is, of course, definable. In others there may be found underlying toxic or metabolic changes which may be considered responsible for the abnormal mental state. On the other hand, there are other psychoses in which none of these factors are determinable, the causation being found in a purely functional psychic factor, psychogenic. In previous clinics you have been shown cases illustrative of these psychoses wherein the organic, toxic, metabolic, or psychogenic factor in etiology was clearly demonstrable. Of hysteria, no organic disease of any part of the nervous system is considered an essential causal factor. It is true, of course, that organic disease may exist in an incidental relationship. The almost uniform usage of the term "functional neurosis" recognizes this attitude. The hysteric may show convulsions or paralyses superficially indicative of organic causal lesions which, however, examination demonstrates to be absent. Although it is true that the psychoses, with greater frequency than the neuroses, are associated with some demonstrable physical factor as causation, it certainly is a far from infrequent observation that the neuroses may have their apparent starting-point in some acute infectious disease, metabolic disorder, physical trauma to parts of the body other

than the head, or physical disease of debilitating character. Again, though it may be true that psychoses offer a less favorable prognosis as a group, it is an equally true and well-known fact that many psychoneuroses persist throughout a lifetime. However, as with the psychoses, so more frequently with the psychoneuroses, do we meet with cases in which none of the physical factors are present. In other words, the demarcation is not so clear and actual as it is arbitrary and variable, and divisions are made depending upon the viewpoint held.

The psychoneuroses are numerous in type and variety, yet it is possible to recognize certain leading symptom groups of which the numerous types set forth by many are but unessential clinical varieties. This is not the occasion to enter into this nosologic controversy or to discuss the various theories proposed in explanation of the psychoneuroses as a group. Of the three main types, neurasthenia, psychasthenia, and hysteria, it is the last which we will consider.

Regarding etiology, with rare exceptions, a predisposing constitutional element is present as the groundwork upon which the symptoms may develop. Physical and psychic trauma, constituting shock, are to be accredited with a rôle of prime importance. Acute infectious disease, debilitating conditions, and toxemias may be the inducing factor. It must be remembered that various evidences of so-called "nervousness" accompany many physical diseases of medical or surgical character. Such "nervousness" more frequently presents suggestions of neurasthenia, though hysteric manifestations are not uncommon. All too frequently hysteric manifestations associated with organic disease of the brain lead to a premature diagnosis wherein the functional feature is overemphasized and, as a result, the organic condition is entirely overlooked. Hysteria may develop in early childhood, more commonly then between the ages of seven and fourteen. With the old idea that hysteria was due invariably to some uterine displacement, it became exclusively a disease of women, but our experience during the World War demonstrated that, if anything, the condition occurred more frequently in men.

"Hysteria" is a term which has been so long used, and so loosely used, and has come to mean so many different things, that a careful consideration of it in its more limited and restricted meaning is quite essential and important. As was pointed out to you a few minutes ago, whether you wish to consider it a psychosis or a psychoneurosis makes no essential difference so long as it is understood that it is essentially a mental disorder usually possessing more features of the psychoneurotic character, but occasionally presenting certain phases which make its differentiation from unquestioned psychoses an almost impossible task. The symptoms of hysteria are so manifold and varied that we can present and illustrate only a limited few on this occasion by the several patients which have been selected for this clinic. Among the mental symptoms should be mentioned that of emotional instability and lability. Without apparent reason there occur the most rapid fluctuations in emotional tone with gaps and jumps from one extreme to another. Not infrequently such changes are popularly known as temper. Suggestibility is possibly one of the most fundamental features of hysteria, so much so that Babinski has defined the disease as a condition which is caused by suggestion and which can be cured by persuasion, pithiatism.

Seen from the standpoint of the psychiatrist, the mental attributes stand in the foreground, the neurologic manifestations, which we will next mention, being given a secondary place. These neurologic, objectively demonstrable, pathologic manifestations, which are referable primarily to the mental state, disclose themselves in the sensory and motor spheres. We meet with many varieties of sensory abnormalities, particularly anesthetics, analgesias, and paresthesias. These sensory disturbances may be rather broadly distributed or localized. The hemi-anesthesia described by Charcot, though denied by others, is a common form of disturbance. Sensory disturbances limited in distribution to parts where covered with stockings or gloves are at times very striking, the so-called glove and stocking anesthesia. Hyperesthesias referable to certain particular points have been described from the days of Charcot and have

been designated as "hysterogenic zones." Among these should be mentioned the region of the ovary, the breast, and other points where it was, a long time back, claimed that pressure exerted would reproduce the hysteric attack. The results from such pressure are to be looked upon as evidences of the hypersuggestibility of the hysteric and not as otherwise causal of any attack. It is in the so-called major attacks of hysteria that we meet with the marked motor disturbances, namely, the convulsions and paralyzes. The convulsions of the hysteric are at times confused with those of epilepsy, but differ, in that the aura is absent, the prodromal period is longer, the convulsion itself more prolonged, consciousness not so deeply clouded, and the postepileptic states absent. Tremors of fine or coarse choreic character occur. The paralyzes may involve one side in hemiplegic fashion, one extremity only, or, more commonly, both lower extremities. These may simulate apparently like conditions of organic causation, but neurologic examination fails to reveal those other changes, usually associated with organic disease, such as pathologic reflexes, muscular disturbances, and the like. Examination frequently does show, aside from the cutaneous sensory disturbances, absence of corneal, conjunctival, and pharyngeal reflexes.

The course of the disease is variable with the type and the individual. At times hysteric manifestations not having developed to a full degree of fixation are rapidly and readily removed by appropriate methods. Chronicity is not known. The constitutional undergrowth, permitting the development of hysteria, remains always even in the face of remissions or the apparent disappearance of symptoms. The matter of diagnosis is frequently a difficult problem requiring a careful individual study of each patient as a distinct personality. The difficulties which beset one's pathway in this regard are better understood through the medium of illustration, and we will, therefore, reserve our remarks on this phase of the subject until we take up the discussion of the cases presented. With regard to prognosis we must differentiate between the deeply rooted hysteric constitution and the more superficial hysteric reaction or epi-

sode. One cannot reasonably expect an underlying constitutional anomaly to disappear or greatly alter, whereas the hysteric reactions are but transient in their duration. This difference will be noted in certain of the patients now to be presented.

**Case I.**—White girl, age sixteen, single, presenting a constitutional psychopathic make-up upon which developed a hysteric reaction in association with hyperthyroidism suggesting the possibility of a toxic thyroid psychosis.

As this young girl whom you are about to see reacts very strongly to any unusual circumstances, this reaction consisting mostly of fear with crying and agitation followed by depression, we shall first review her history briefly before presenting her to you. Incidentally, it may be advisedly remarked that, with the personality exhibited by this patient, it is not without considerable danger of unfortunate suggestion that her case be discussed within her hearing.

She was first brought into the hospital and the surgical service of Dr. John McHale Dean because of symptoms indicative of renal involvement and a very evident goiter. On admission temperature was normal. There was a history of pain in the region of the left kidney beginning two weeks before and which within the few days preceding hospitalization radiated down the front of the left thigh. There were chilly sensations and sweats. Physical examination showed tachycardia (120-150), very much enlarged thyroid, the neck measuring  $12\frac{5}{8}$  inches in circumference. This enlargement was general, involving all lobes, the swelling was soft and pulsating. No indications of exophthalmos. Uterus was small, pelvis was negative. Remainder of general physical examination was negative, other than that patient was rather sallow in appearance, the skin being cold and clammy, evidently undernourished. It was noted that she was "extremely nervous, inclined to be hysteric." The urine was of low specific gravity and on one occasion showed a trace of albumin, but was otherwise negative. Leukocyte count was 16,600 and on the following day 13,600. Blood Wassermann was negative. Basal metabolic rate was plus 125 per

cent. x-Ray of urinary tract showed no opaque stones in either ureter, kidney, or bladder area, and kidney appeared normal in size and position. The patient's general condition remained about the same for about a week with the exception that the pain referred to the left kidney region, at times severely intense and requiring morphin, lessened and disappeared entirely. The tentative diagnosis of acute pyelitis was relinquished and the question of operative treatment of the thyroid was up for action. She had received sedatives continuously since admission.

At about this juncture, associated with a sharp rise in temperature to 100° F. and pulse to 140, the patient became very much disturbed, restless, crying out loudly, screaming, and refusing food. She was only partially subdued by the exhibition of opiates. Throughout this night she continued extremely restless and agitated, continuously scratching different parts, but particularly the abdomen, and picking in a purposeless, "nervous" manner at her fingers and hands. Along toward morning she announced with much wailing and weeping an entire loss of vision, and insisted she was completely blind.

A neuropsychiatric consultation was requested. It will be well at this point to briefly review this patient's past history from a mental viewpoint. In the first place, we find nothing grossly evident or distinctly psychopathic in the family history. We have no record of how long the goiter had been present. The patient has lived all of her life in a not far distant small country town, had never been away from her home, and never separated from the parents and family. She has passed her sixteen years in more than the usual drab existence of a small village. Though her life was without specific difficulty or note, she has always been looked upon as delicate and weakly. She has not shown the normal tendency toward association with others of her age. For a few years past she has been given to having spells of crying and depression of short duration, and two years ago had what the mother calls a "fainting spell." She has not been backward intellectually, having kept pace with her environment and opportunities in this respect. Menstrua-



tion was established at the age of fifteen, has always been irregular in occurrence, lasting from four to six days and associated with pains and discomfort. The last menses was over two months ago. We will now have the patient brought in for examination, but will withhold our discussion until after her removal.

As mentioned before, it is not always well to discuss your findings too fully before the patient, but now that she is gone we will review the important features. The pupils were dilated but equal and normal in light and accommodative reactions. Though the patient asserted she was blind, you noted that objects brought suddenly before her eyes caused a closing of the lids. Also, it was noted that she would at times move her eyes in the direction of a stimulus like a person seeing. Other cranial nerves were negative so far as could be determined without better co-operation from the patient. Sensation to pain and light touch (pin prick) was hyperacute over the entire trunk and extremities. Motor system showed no paralysis or other abnormality excepting for marked restlessness and continuous picking at the fingers and hands. The tendon reflexes were all exaggerated, but equally so on the two sides, and no pathologic reflexes were obtained. There were no signs indicative of organic disease of either the central or peripheral nervous system. On the mental side the patient was found resistive, non-co-operative, and, to a large degree, inaccessible. She would answer questions occasionally, but usually with the same repeated expression, "I could not say, doctor, please." An investigation of orientation, insight, and other subjective mental states met with similar success. When she spoke at all, it was in low whining tones and unintelligibly most of the time. She did grasp some questions asked and followed some simple directions correctly (such as Put out your tongue, etc.). Some remarks were to a definite degree illogic and irrelevant. No complaint of pain could be elicited and the patient volunteered no information spontaneously. I forgot to mention that, in view of the complaint of blindness, an eye examination was made today by Dr. John Green, Jr., and this revealed no evidence of any pathologic



findings in the eye-grounds. The opinion as to the mental condition may be stated as follows: The mental condition is very suggestive of hysteria. The history indicates clearly a constitutional psychopathy as a basis for this reaction. There is also unquestionably a toxic thyroid. This is not a typical thyroid toxic psychosis, but there is sufficient indication that the thyrotoxicosis has acted to light up a fundamentally psychopathic constitution and the present hysteric reaction.

The essential features in this case are two: The hyperthyroidism and the acute mental disturbance. The questions raised were: "Is the mental abnormality due to the thyrotoxicosis or not? In either event, is surgical intervention indicated? When we look back into the mental history of this patient we find evidences of a constitutional psychopathic disorder shown in instability of emotional control, lack of outward interests of a normal type, an introverted, self-retiring temperament. This is all of the groundwork necessary for the hysteric constitution and out of which the hysteric attack may be expected to grow under the pressure of stress. The goiter had been present for some time past, but the acute mental upset did not occur until after a week in the hospital. Remember we have here a country girl, never away from home, never away from parents, abruptly picked up and transplanted to an entirely new, unfamiliar, and frightening environment. She was physically sick and ill at ease. Among strangers and with entirely new experiences piling up rapidly, many physicians, many examinations, the taking of blood and of urine, x-ray exposures and talk of operations, a large element of fear developed and pushed into active open view her constitutional tendency toward hysteria. If you will remember her reactions you will recall their childish simplicity. She answered questions in an incomplete manner in low, whining tones and yet she did understand and obey simple directive orders. The psychoses caused by hyperthyroidism are not often so fulminant in their development and are usually associated with a greater degree of confusion, possibly with depressive or paranoid coloring. They present, in other words, more the appearance of the toxic psy-

choses as a class. Actual confusion was not present in this case and there were no other symptoms of a toxic psychotic state. By exclusion then we conclude that we are dealing here with a hysteric reaction. As to operative interference at this time, I think we can easily agree that such would be unwise. This is so because the thyroid condition does not appear to be the causal factor, because the mental upset at present is too acute in its manifestations, and because, most of all, we may confidently expect that this severe mental reaction will subside rapidly and have largely disappeared within the next few days. Then surgical treatment will be in order as in any similar thyroid disease. We will hope to present this patient again at a later clinic.

*Second Presentation.*—From this patient's appearance today you may scarcely recognize her as the one you saw at our clinic three weeks ago. The day following that clinic the active mental symptoms, then so evident, practically disappeared, leaving about as abruptly as they came, and within the next three days she had gone back to *her* normal state. A two-stage thyroid operation at ten-day intervals was done by Dr. Dean, the arteries of the right side being ligated at the first and of the left side with partial thyroidectomy at the second. The post-operative course has been uneventful and the patient is now to go home, to return at a later date for further operative treatment. There has been no return of the frank hysteria, and so far as that is concerned she has recovered, though, of course, the hysteric constitution remains as formerly.

**Case II.**—White girl, age eighteen, single, with hysteric convulsions and psychotic disorders, Jacksonian epilepsy and an intracranial growth brought into question.

This patient was admitted to the surgical service of Dr. John McHale Dean, members of her family having gotten the idea that some operation on her head would cure her disease. So far as can be learned the family history shows no abnormal mental states. Menstruation was established at about thirteen was then absent until fifteen, since when it has occurred irreg-

ularly and scant, but invariably with an aggravation of all symptoms. It is stated that the patient has become mentally dull within the past year.

The record shows that "fainting spells" first occurred about seven years ago shortly following the death of her father, to whom she was closely attached. She was then eleven years old. It is also recorded that she had some "jerky movements" of all extremities for several months before the first attack of unconsciousness. In her "attacks" she falls down, froths at the mouth, sometimes bites her tongue, and otherwise injures herself. There has been no loss of control of bladder or rectum. It was stated that these attacks always begun with a jerking in the left hand and arm, but otherwise without warning aura. The attacks lasted from five to ten minutes. Upon this history a tentative diagnosis of epilepsy, possibly Jacksonian, was made, and examinations were directed along this line of attack.

General physical examination reveals a rather poorly nourished girl of the tall and slender type, the hands are long and slender, general type eunuchoid. There is some fullness of the thyroid gland, but no indications of an exophthalmic goiter picture. The eye-grounds show nothing pathologic according to Dr. John Hardesty. Dr. P. F. Kistner reports an intumescent rhinitis and deflected septum, but otherwise no otolaryngologic abnormality. x-Ray of the skull by Dr. Sante shows the anterior and posterior clinoid processes abnormally closely approximated, with the sella turcica normal in size and shape. The basal metabolic rate was plus 20 per cent. The urine shows a trace of albumin, but is otherwise normal. Neurologic examination shows that the cranial nerves were negative excepting that the pupils were enlarged, dilated, and slightly irregular, reacting to accommodation and light but sluggishly. Sensation to light touch and pain is acute and normal everywhere over the trunk and extremities. Muscular tone and development is good with no atrophies, hypertrophies or limitations of active or passive movements; there was no tremor, no inco-ordination, no weakness. The deep tendon and periosteal reflexes, both upper and lower, are all much exaggerated, but equally so on the

opposite sides. There is a pseudopatellar clonus, a suggestion of Chaddock's sign, but no positive pathologic toe signs. There is a marked plantar defense reaction. Abdominal reflexes are active and equal. Jaw-jerk is present, Chvostek is absent.

Mentally during the period when patient is not in an attack she presents no gross psychic abnormalities, is correctly oriented, memory is not impaired. She answers questions simply but with no delay. Gives a fair account of herself in a manner such as a child might use. The intellectual level is not commensurate with her age, but this is better explained by a lack of education than by actual deterioration. There are no delusions or hallucinations. Consciousness is not clouded, but there is a slowing of thought processes. Emotional tone is lowered, she is to a degree apathetic and indifferent, but not depressed. There is no anxiety or apprehension. Insight into her condition is only partial.

While in the hospital during a period of a little over three weeks this patient has had "spells" nearly daily, and on some days several. The nurse would find the patient unconscious to a degree that she could not be aroused. The whole body twitched and jerked, the patient frothed at the mouth. The finger-nails and lips were cyanotic. These attacks lasted about fifteen minutes and were sometimes followed by a deep sleep. On one occasion patient was seen shortly before the onset of an attack. She appeared somewhat confused and dazed, obviously did not fully grasp surroundings, although she answered questions properly and correctly. A few minutes later she became very greatly excited and disturbed, was extremely noisy, screaming loudly in a sing-song fashion. There was a tendency to throw the body about the bed, she actively resisted all passive movements. She assumed a position of marked opisthotonos. The eyes remained open and she would note persons enter her room, would take in and comment on events transpiring about her, noting minor affairs going on about her in her rather steady though disjointed, distracted, and rambling logorrhea. This condition continued for about a half-hour during which there were no local or general convulsive movements, no loss of bladder or

bowel control, no injuries to self. She then became more quiet, but continued resistive, inaccessible but talking, moaning, and crying, lamenting her illness, referring to its beginning shortly after her father's death, calling by name some of the nurses about her. Gradually she became quiet under opiates, but at no time had the condition entirely subsided before she was removed from the hospital some seven hours later because of the disturbance to others created by her excessive noisiness.

As we look backward now over the course of this case we find a number of features of particular interest. First, we are dealing here with a patient who has exhibited an abnormal neuropsychic make-up for several years past, a large portion of her entire life. Owing to the fact that we have a rather inadequate history and further investigation is quite impracticable, we are left somewhat in doubt as to the origin of this condition and its development during the past few years prior to her coming under immediate observation. So far as can be learned the spells with convulsive attacks which we have described had not until recently been seen by a competent observer. It is evident that the description of these as given by the family could not have been entirely accurate, at least, not entirely complete, and it is also evident that on the basis of these inaccurate and incomplete descriptions it was thought that possibly there may have been some intracranial involvement in the nature of a tumor. It was on account of this assumption that she was sent into the hospital as a surgical case. The assumption that there was some intracranial involvement led to the conclusion that this was a case of focal epilepsy, this conclusion being somewhat bolstered up again by the family reports that the convulsive attacks had started with movements in the left hand. From this arose the tentative diagnosis of a Jacksonian epilepsy. However, when we come to go over this case carefully we find that there is no other evidence whatsoever of a Jacksonian condition than the reported movements beginning in the left hand. Neurologic examinations failed to reveal any signs whatsoever of intracranial or other central nervous system organic lesion. There were neither general nor specific symptoms

or signs which could in any way be attributed to a brain tumor. So that now we have left the differentiation between a true idiopathic epilepsy and convulsive attacks of a hysteric character.

This case illustrates very well that the description of attacks simulating epilepsy, as given by incompetent observers or by nurses, as a rule is not sufficient that a diagnosis of epilepsy may be made, much less for the differentiation of this condition from its simulator, hysteria. In the attacks which we had the opportunity of personally observing, there was a prodromal period of confusion and dazedness lasting for some minutes. Then the attack began with screaming, crying, and similar disturbance without convulsive movement of any part of the body. Later, during the height of the attack, the patient was not unconscious, recognized the nurses and others about her, rambled along in a disconnected, disjointed logorrhea, did not injure herself or lose control of her bladder or rectum, threw herself about the bed in a clumsy, awkward fashion, but without doing any personal injury, and at other times assumed a marked opisthotonic attitude, resisting all passive movements. Again, this condition kept up for hours instead of lasting but the few minutes of the typical epileptic attack. In this condition of excitement, lasting as it did for several hours, we see in this case a much nearer approach to a true psychotic condition than in other cases which we will consider during this clinic. Seeing this patient for one time only, and without any records while she was in this condition, might give rise to a very great deal of difficulty in differentiating this condition from a psychosis, and the case illustrates perhaps in the end the lack of practical value in attempting to make any such differentiation.

We should, perhaps, comment here before closing this case upon some of the physical findings. There is, in so far as relative body measurements are concerned, an evident preadolescent endocrine disturbance. This is indicated by the long slender type, eunuchoid characteristics, disturbed menstrual function, and thyroid involvement. We have here probably a certain

degree of hypopituitarism, a lack of function primarily of the anterior lobe, together with hypogonadism, possibly secondary to the preceding and a slight, probably secondary, involvement of the thyroid gland function. In the last analysis we may safely conclude that we are dealing here with a hysteric constitution upon which have been built hysteric attacks over a period of years and these associated with motor disturbances of a convulsive nature. Because of the long duration of this diseased state and its strongly constitutional groundwork, the prognosis for recovery is distinctly poor.

**Case III.**—White woman, aged twenty-nine, married. Clinical signs suggestive of spinal cord lesion for which laminectomy had been done followed by intensification of complaints. Hysteria.

This patient was referred by Dr. William Engelbach for investigation of the mental state and its bearing upon a possible organic disease process in the central nervous system. We will give in brief abstract here the essential features of the history and examination before proceeding to the discussion.

*I. History.*—*A. Present Illness.*—*1. Complaints.*—Numbness and inability to use the right foot, with impairment of gait and station. Numbness of upper extremities, especially hands. Pain in interscapular region since operation. Attacks of crying and laughing. Fatigability.

*2. Development and Course.*—Symptoms were first noted, perhaps about three years ago, but definitely as far back as a year and a half ago when she noticed some disturbance of the right foot, an awkwardness and inability to use it properly, but continued with her work as seamstress, running a foot-power sewing machine. This condition continued until May, 1923 when an operation on the upper dorsal spine was performed at the Barnes Hospital by Dr. Sachs. Since that time she has complained of the symptoms becoming much more exaggerated, to such an extent that she cannot walk without a cane or support because of weakness and lack of co-ordinating control. There has been a feeling of numbness in both hands, but never any



weakness. She has been examined by a number of physicians in St. Louis within the past year and a half. On April 7, 1923 she was examined by Drs. Frank Fry and L. B. Alford, who report "She was evidently abounding in hysteric reactions and, furthermore, we found no focal organic signs."

*B. Personal History.*—White female, Jewish race, age twenty-nine, married nine years, two boys, one eight years old and the other five, living. There was one miscarriage about four years ago. Three years ago her husband left her and she was forced to work and support her children. In early life she had scarlet fever and measles, but with no serious complications. Attended school in Russia and had a private teacher for a time, but has not had much education. Has lived in the United States for about ten years. Employed at dressmaking, but at present time is unable to do any work. No addiction to alcohol or drugs. There has been no pain in any part of the body prior to operation. Menstruation was established when she was fourteen years of age, five to six days' duration, without any abnormal symptoms, occurring about every twenty-six or twenty-seven days regularly. No history of previous attacks or nervous disorders similar to the present illness. There has been a general increase of weight within the past eighteen months.

*C. Family History.*—Negative so far as any bearing upon the present illness of the patient can be ascertained. No record of nervous or mental disorders in the family.

*II. Examination.*—*A. General.*—Nutritional state and development good, of short stature (height 62 inches), rather obese, (weight 160 pounds), no deformities of bones or extremities, slight dorsal padding of fingers, which are short and tapering. Adiposity is chiefly of pelvic girdle type. Blood-pressure 108/70. There is a linear operative scar from the second dorsal spine downward about 7 inches under which the spinous processes are not palpable. Head of average size and conformation, no tenderness over the skull or sinuses. Thyroid slightly enlarged. Physical examination otherwise shows no gross indications of abnormality of visceral function. Basal metabolic rate plus 8 per cent. *x-Ray* examination shows absence of the



spines of fourth, fifth, sixth, and seventh thoracic vertebrae with suspected wire fragments in this area. Otherwise negative. Hemaglobin and blood-cell count normal, blood Wassermann negative.

B. *Neurologic*.—*Sensorimotor*.—(a) *The Cranial Nerves*.—Smell is acute and normal. Visual fields and acuity are not limited. Ophthalmoscopic examination negative. No diplopia, nystagmus, ptosis, or palsy. Pupils are equal in size and regular in outline. Motor and sensory cutaneous V normal. No asymmetry, palsy, or tremor of the face. Hearing is acute and normal. Rinne and Weber tests normal. No vestibular signs. Taste objectively normal. Tongue protruded in midline, no tremor, no speech defect other than that due to difficulty in use of English language.

(b) *Sensation*.—Everywhere acute and normal, excepting over the lower extremities from the knees downward. Over the right lower extremity sensation to pain, light touch, heat and cold, and vibration is more acutely and accurately perceived than over the left lower extremity in similar areas. There is no anesthesia in any locality. She complains of numbness and dulness of feeling subjectively in this area.

(c) *Motor System*.—Muscular development and tone fair, rather flabby, considerable adipose tissue. Strength in the upper extremities is good. Apparently some weakness in the lower right extremity, no inco-ordination. In walking the gait is best described as the unsteadiness of one who is drunk, there being a tendency toward reeling on the right and an awkward throwing out of the right foot in attempting to walk. Station is unimpaired in the standing position and in bending over. No Romberg.

(d) *Reflexes*.—Pupils react to light normally and to accommodation normally. Tendon reflexes in the upper extremities are active but equal on opposite sides. There is a double Hoffmann. No wrist sign. Right knee- and ankle-jerks are very distinctly more than those on the left. There is a knee-clonus on the right, fairly well sustained and also an ankle-clonus on the right less persistently sustained. No Babinski or Gordon.

There is a definite Chaddock on the right. Abdominals are absent.

C. *Psychical*.—Patient presents nothing unusual in appearance and behavior other than what might be attributed to racial characteristics. She answers questions freely, talking about herself and her illness in considerable detail, and at times being difficult to interrupt. Attention is very well gained, held well to her present difficulties, but not so well to subjects in general. Orientation is not disturbed. Memory is normal. There is no clouding of consciousness, no delusions or hallucinations. Emotional state is most of the time neutral, at times she shows a slight depression when recounting her difficulties of life, especially regarding her domestic situation and the children, and shows a slight tendency toward weeping.

III. *Conclusions*.—Repeated examinations have shown no abnormality of the cranial nerves. There has been found a disturbance of cutaneous sensation over the lower extremities below the knees, there being a difference in acuity of sensory perception on the right and left leg with a diminution on the left. Motor system shows no atrophy, gait is impaired by an unsteadiness which is not characteristic of any tract or system disease. Reflexes have been found increased in the right lower extremity with persistent Chaddock.

In summing up these findings it is impossible to explain these apparent signs of organic disease by any definite or localized lesion either in the spinal cord or the brain. The Hoffman and Chaddock reflexes have been observed in individuals otherwise normal and in whom other accompanying signs or symptoms of nervous system disease are absent. The knee- and especially the ankle-clonus is suggestive, but not finally conclusive of organic disease, as these have varied from day to day with a tendency toward a steady decrease. The distribution of the sensory disturbance does not in any way correspond to that occasioned by an organic disease, whereas, on the other hand, it does correspond with similar disturbances found in hysteria. So far as any tumor of the spinal cord is concerned, or so far as any root irritation is concerned, it is significant that, although

this condition has existed for a year and a half, there has not been any complaint of the pain customarily associated with such cord conditions. What rôle the operation of five months ago may have had in the causation of these apparently pathologic reflex findings is at this time purely speculative. At best it can be said that they suggest the possibility of an organic condition somewhere in the pyramidal tract. However, it is believed that the greatest part of this picture is best explained by a diagnosis of hysteria.

From the mental standpoint this patient exhibits a considerably different situation from the two which we have previously seen. Here the apparent physical disability is the outwardly prominent feature of the case. The mental symptoms do not in any way take on the character of psychotic disturbances, nor does the woman present any gross evidences of active mental disorder. Her entire attention primarily was focused upon the disability of the right foot and leg with the weakness and consequent inability to carry on her work. It should be remembered that for some months prior to the development of this weakness she had been intensely worried and depressed over domestic difficulties and the burden of properly caring for her children. This burden became more and more impossible in her mind as her sickness and inability to work efficiently became more and more pronounced. There was here established a distinctly vicious cycle. Finding no relief after consulting a number of physicians, she was led to pin her hope upon the result of operative treatment. Our examination and history does not at this time reveal what indications there may have been for operation at the time it was performed, nor can we determine why the particular site of operation was selected. At all events, following the operation, the patient has not improved so far as her own subjective state is concerned, and she, in fact, claims that she has become much worse and less able now to care for herself than she was before this treatment was undertaken. However, there is really no indication that the operation has in any way acted detrimentally from a physical viewpoint, although it obviously has exaggerated her mental attitude toward

the entire situation. It has to this extent assisted in the confirmation of her fear that nothing will ever be done to make her recover her previous health.

Her whole make-up is of a psychoneurotic type and in addition to this, the absence of any definite or clearly indicating neurologic signs which might lead to the localization of any central nervous system lesion leads us by exclusion to arrive at the diagnosis of hysteria. Regarding the prognosis we have a somewhat clouded situation also. This condition has now been going on for a good many months and has by this period of time, as well as the lack of effectiveness of any treatment applied, become to that degree more fixed and stable. With proper handling and treatment it is believed that with sufficient time a practically complete restitution to her normal can be accomplished.

**Case IV.**—White woman, aged forty-two, single, presenting symptoms of a hysteric character associated with the menopause, but ideation suggestive of an involuntional melancholia.

This patient was first seen a couple of weeks ago in consultation with Dr. McNearney, the history and examination at that time being briefly as follows:

I. *History.*—A. *Complaints.*—Patient complains of a throbbing in the head, poor memory, inability to concentrate, and nervous spells.

B. *Development and Course.*—The present trouble began about six weeks or two months ago, following a severe cold, after which developed a throbbing headache. The actual pain of the headache has since disappeared, though the throbbing of an annoying character has persisted. During the past few weeks she has become increasingly more nervous and recently has been described as having spells during which she talks irrationally and expresses certain ideas, seemingly of a delusional character. These spells are of short duration. She believes that she is lost (religiously) and that others are trying "to get her." Some few weeks ago she was in the hospital under Dr. McNearney's care, x-ray examinations were negative as were the

Wassermann and other routine laboratory tests. General physical health has remained fair, although there has been some loss of weight. There has been no constipation. Spells recently have become more aggravated, so that the family are concerned over her condition and fear that they cannot take care of her at home.

C. *Personal History*.—Age forty-two, white female, previous life has been negative so far as can be ascertained up until the onset of the present illness, there having been no serious physical diseases or previous attacks of mental disorder. Menstruation was established at about the usual age, having occasioned no trouble. Has been regular until within the past several months, when it has been coming somewhat later than usual and, incident to its appearance, patient has been somewhat more nervous, as she expresses it. Occasional periods in the past few months have been missed. There have been the so-called hot flushes and other complaints incident to the menopause.

D. *Family History*.—Is negative so far as can be ascertained as having any bearing on the present condition.

II. *Examination*.—General physical examination reveals nothing grossly abnormal. General nutritional state is good, there has been some loss of weight, but this is not evident in any degree of emaciation. Neurologic examination shows pupils dilated, but equal, reacting normally to light and accommodation. Other cranial nerves are negative. Tendon reflexes are present, exaggerated somewhat, but equally so on the two sides. No pathologic toe signs. Sensation is acute and normal everywhere over the trunk and extremities. There is no disturbance of motor activity, strength is good and equal, no paralyzes or hypertrophies, no tremor, no inco-ordination, no ataxia.

Mental state: Patient presents a rather normal appearance on casual observation and answers questions fairly readily, but shows a tendency to conceal some information concerning herself, at least not being perfectly free in her accounts of the spells as described by members of the family. Orientation is not disturbed in any respect. Memory for remote and recent events

is clear. There is no clouding of consciousness, no confusion. No definite delusions or hallucinations are elicited. Emotional state is rather neutral with no evidence of depression or elation. She is quiet, answers questions fairly readily, but with some reluctance, as previously mentioned. Insight into her condition is fairly adequate and she has some appreciation of the fact that her mental activity is not entirely as it should be. The spells spoken of tend to occur in the early morning hours when she becomes quite confused, talks incoherently and irrationally concerning various things, especially of a religious nature. It is learned from her that she believes that she is lost because she has not attended church regularly recently, and she thinks that other members of the family are lost for the same reason. This morning early she was slightly upset and fearful because she thought that someone from some other part of the apartment building in which she lives was coming in to "get her." When questioned about this now she admits she thought this, that she was somewhat fearful, but that she does not know who it is, nor does she know of any reason why anyone should wish to harm her. Otherwise no definite delusions can be elicited. No hallucinatory experiences have been established at any time.

III. *Conclusions.*—In the absence of any physical or neurologic disorder determinable by examination, the age of the woman, with the history of irregularity in menstrual function, the character of the mental symptoms with their variation and lack of actual confusion, with partial insight and variable course, indicates a menopausal disturbance of hysteric type. It was recommended that the patient be immediately hospitalized for further observation and treatment.

Since under observation in the hospital this patient's mental state has altered considerably, showing definite variation and raising questions concerning the diagnosis and prognosis. For the first few days after her admission her condition showed no essential change from that which had been reported at home. The periods of mental disturbance and agitation occurring early in the morning continued. Then the patient began to be more impressed with the depressive delusions that she was lost and

that her family were lost owing to the sins which she herself had committed in the past. This auto-accusatory element became very prominent. Along with this there was a marked degree of restlessness, agitation, and insomnia. She slept but little, even under the influence of opiates. She was continuously out of her bed, walking about the room, showing evidences of fear and anxiety. She knelt upon her knees praying for hours, moving about over the floor in this posture, producing excoriations and abrasions over the knees. She was sure now that she was lost and offered the hospital attendants what money she had if they would kill her. She spoke of suicide and said she wanted to die, but in the next breath would state that she would not think of doing any such thing as that. Throughout all of this agitation she did not show an accompanying affective depression which was proportionate to the ideation expressed.

Although there were at times some slight tendencies toward confusion, she was always able to recognize those about her, talked rationally enough about subjects other than her own sins and the like, and was never disoriented excepting for a day or two as to time. Up until today there has never been evident any sign of retardation or difficulty in thinking, although she herself has complained of such a feeling. The delusions have been entirely of this self-depreciative, auto-accusatory character with reference to sins which she has committed, but which she herself, upon questioning, admits have been of trivial character. Agitation and restlessness reached such a grade that for a couple of days it was necessary to use mechanical restraint to secure for her a proper amount of rest. While thus restrained, it is significant to note that she remained quietly in bed and subsequently, after the restraint was removed but kept in the room within her vision, she would continue to remain in bed without difficulty. After three or four days of this agitation, she quieted down again and has since remained in bed for the past three days without difficulty. She takes food better, does not present the appearance of confusion and anxiety previously noted, rests much better throughout the entire night, but still gives expression to her auto-accusatory ideas and her firm conviction that she



herself is lost. At times, however, while making these statements she will smile in a rather normal manner.

As you see her today she is quiet, presents no grossly abnormal appearance, talks rather normally about subjects in general, shows no evidence of confusion or clouding of consciousness, no indication of delusions, and outwardly no great appearance of depression. However, she does today seem to be somewhat retarded. As you will notice, she answers questions more slowly and less completely than she has in the past, and is still convinced of her own sin, unworthiness, and damnation.

This patient is presented to you today with her history to illustrate the excessive difficulty with which we now and then meet in differentiating hysteria from a definite psychosis. Here we have a woman in the devolutional period and who, from the clinical history, is apparently well begun in the menopausal change, who developed, following an acute infectious condition of the respiratory tract, an abnormal mental reaction, at first of no great degree of acuteness, but later taking on more definitely psychotic features. At the present time we are confronted with the problem of differentiating this condition, which has certain indications of hysteria, from one of those depressive psychoses occurring during the devolutional period and particularly involuntional melancholia. The observation that this abnormal mental condition had its origin somewhere about two months ago and has not up until the present time developed more definitely than it has along psychotic lines, is possibly significant and of value in making a diagnosis. Also, in the course, the extreme variability with fluctuation, the lack of marked confusion, the retention of a certain amount of insight, the absence of definite hallucinations, and the, at first, poorly fixed delusional ideas, suggest more strongly the possibility of a hysteric reaction at the menopause than any other type of disorder. However, this conclusion is somewhat clouded by the very marked auto-accusatory content of the delusional ideation, this indeed, taking on very strongly the involuntional characteristics. The discordance between the ideation and the emotional state, that is, the lack of outwardly expressed de-



pressive features, speaks against an actual affective depression. And yet within the past few days, especially today, there has been more evidence of this depression than formerly, together with some degree of retardation. The absence of any previous history of mental disorder in the individual suggests strongly that it is a reactive condition at the time of the menopause, possibly a manic-depressive psychosis, possibly an involutional melancholia, but as yet the balance is in favor of an episodic, hysteric reaction occurring in association with the climacteric. The prognosis cannot at this time be made safely, but if our diagnosis of hysteria is correct we may look forward to a favorable outcome.

**Case V.**—White girl, aged twenty-five, single, presenting symptoms of major hysteria with motor disturbance and, in later developments, suggesting strongly the possibility of dementia præcox.

This patient was first seen in 1918 in consultation with the late Dr. Louie Butler, and again recently upon the request of Dr. Alphonse McMahon. The original record of history and examination made in 1918 reads as follows:

*Anamnesis.*—September 22, 1918: Family history is negative for nervous and mental disorders, so far as is ascertained. Mother is of a somewhat neurotic make-up.

Patient has always been in fairly good general physical health, never having had any serious physical diseases. She has, however, always been of a nervous, somewhat high-strung temperament, inclined to disagree with parents and others and to have her own way. Several years ago she had a fall, and the mother believes that this supposed injury to the lower part of her spine has something to do with her present condition, as she has apparently been more nervous since that time. The injury itself was not severe, apparently consisting only in the patient's having sat down rather too suddenly and hard. Menstrual function was established at the age of fifteen and has never occasioned any particular trouble other than that incident to the present illness there has been more or less irregularity

with amenorrhea. She has been under the care of several physicians in the several years past, and it seems to be the final opinion that there is no gynecologic or other physical disorder. She has also been treated by chiropractors and osteopaths, either one of which claimed that she had some gynecologic disorder and treated her for a long period of time by vaginal massage.

Dr. Butler first saw the patient about May, 1917. At this time her condition was such that she was in bed. She had certain muscular disorders involving the extremities, neck, and shoulders which led to a diagnosis of myoclonia. At different times during the past year and a half various changes have occurred. At one time, for a period of several days or more, she claimed that she was blind, at another time her speech was entirely lost, at another time she could not swallow and had to be fed. Under Dr. Butler's care she was in St. John's for something over two months, improving considerably, to such an extent that she could be up and about. However, on her return home her condition became as bad as formerly. Her general nutrition has kept up well. For some time past she has been at home in bed under the care of a nurse, although more recently she has been sitting up for an hour or so once or twice a day. The muscular disorder has largely disappeared and affects now principally the neck and shoulders.

*Examination.*—September 22, 1918: Mentally the patient presents a rather normal appearance, although there is some evidence of slight depression in her facial expression. She, however, shows no psychotic symptoms, converses normally, although in somewhat subdued tones and in a hesitating manner, as though possibly somewhat embarrassed. No intellectual defect or sensorial clouding.

Well-nourished white girl, good color. Head of normal conformation, no evidence of injury. No sinus tenderness. No glandular enlargements. Pulse of normal frequency, no vascular changes.

Pupils are equal, regular and round in outline, react to light directly and consensually and to accommodation normally. No limitation of visual fields. Ophthalmoscopic examination

negative. No nystagmus, palsy, diplopia, or ptosis. Taste and smell subjectively normal. No facial palsy or asymmetry. Hearing not grossly disturbed. Tongue protruded in midline, without tremor, no speech defect.

Sensation to pain and light touch is normal everywhere, excepting the lower extremities, where there is a complete anesthesia, the exact upper limit of which was not determined.

Musculature of fair tone, good development. There are noticeable occasional twitchings in the forearm and hands, especially in the supinator regions. Also about the shoulders, neck, and face. These movements are of small amplitude, come irregularly, and are but transient in a given muscle group. Patient is not able to get out of bed without assistance because of alleged weakness in the lower extremities.

Biceps, triceps, radial and ulnar, knee- and ankle-jerks are present, equal, active, but normal. Babinski, Gordon, Oppenheim, and Chaddock absent. Diagnosis: Paramyoclonia, hysteric.

Following the above examination the patient was removed to a private sanitarium away from St. Louis, where she remained until April, 1921, about two and a half years, since when she has remained at home. Since 1918 there have been long periods of amenorrhea with occasional vicarious menstruation. During the past two years there have been two "attacks" lasting for a period of one or two weeks immediately preceding the onset of the menstrual period. She has had but three menstrual periods in the past two years.

The present "attack" began about three weeks ago associated with severe jerking of the muscles of the neck, arms, back, and abdomen, but with no evidence of psychotic symptoms. This motor condition practically disappeared in about two weeks following the onset of a menstrual period, but, at this time, psychic symptoms appeared manifesting themselves chiefly in the form of what was termed by the parents as "flightiness," some incoherence, and delusions. This condition continued to augment until she became unmanageable, insisting upon getting out of bed and then falling. Delusions of a persecutory char-

acter became evident. There were auditory hallucinations, she heard God's voice directing her to sacrifice herself for her sins and thus save her family. She slept poorly, ate practically nothing, and was severely constipated. The foregoing record of the patient since she returned home from the sanitarium was furnished by Dr. McMahon, at whose request she was seen on September 8, 1923. The patient was admitted on that same day to the hospital.

Physical examination by Dr. McMahon was reported as follows:

(A) *General*.—Patient is a well-developed, fairly well-nourished individual, showing some slight loss of subcutaneous tissue about the body. General measurements are eunuchoid. Hands same type. Fingers moderate length, slender, slightly tapering. Palm narrow in proportion to length of fingers. Hands are warm and moist. Feet same character as hands. No edema, cyanosis, or dyspnea. Patient at this time presents some jerking movements of head, upper extremities, slight in trunk. Contractions are clonic in character. These were more pronounced in the original observation. Talking incoherently, but responds to questions, struggling in an effort to free herself from her restraint.

(B) *Regional*.—Head: Normal in contour. Facies eunuchoid. Slight flushing over malar processes. Hair is brown, medium texture.

Ears: Negative.

Eyes: Pupils equal, regular, symmetric, react promptly to light and accommodation. Eye muscles are intact. Constant rolling of eyes during examination.

Nose: Negative.

Mouth: Teeth show several fillings, slight crowding of lower incisors.

Mucous membranes of normal color. There is considerable pyorrhea.

Neck: Thyroid slightly enlarged. No abnormal pulsations. Cervicals, axillary and epitrochlears negative.

Chest: Expansion fair and equal. Slight impairment of

resonance at right apex posteriorly, otherwise negative throughout. No râles, rubs, or adventitious sounds.

Heart: Moderately rapid, regular, synchronous with pulse, free from murmurs and accentuation.

Abdomen: Asthenic type. No tumefactions or visible peristalsis.

No tenderness or rigidity on light palpation. No organic pathology noted.

Vaginal: Not made.

Extremities: Bones and joints are negative.

Reflexes: Normal throughout.

Neurologic examination showed no pathologic changes in any way indicative of any organic disease of the central or peripheral nervous system. Occasionally there have been noted in slight degree the muscular jerkings previously mentioned.

For the following three weeks her mental condition changed but little in the essential details, and she has been much as you see her now with the exception of certain variations from one day to the next. She is apathetic, dull, and inaccessible for the greater part of the time. When not restrained in bed she will get up and fall to the floor, or when assisted to her feet will limply fall. Also, when placed in a chair, unless restrained, she will fall forward to the floor, heedless of bruises thus sustained. And yet, as you will see, her muscular development and general condition offers no explanation for this conduct which by her relatives is attributed to extreme weakness. At first there was an extreme constipation, almost an obstruction, corrected only by repeated purgation and enemata. For two or three days at a time she will refuse all nourishment and then follow this with a period of several days during which she takes food fairly satisfactorily. Note how she resists any passive movement of her arms, how she draws away her feet (and with a good degree of strength too) when we wish to examine these excoriations on her ankles which she has caused by continuously rubbing against the lower margin of the restraint sheet. She turns her head away when we endeavor to get her to speak and closes her eyes tightly when her head is turned to face us. The

skin of the face appears oily and greasy and the complexion is sallow. The feet and hands are definitely cyanotic when pendant, but the hands immediately pale when the arms are lifted above the head. You get today the appearance of considerable mental confusion.

At other times she is brighter and more alert, becoming then more accessible and making fairly rational responses to questions. On one such occasion a few days ago she cleared up considerably, showed that she was well oriented for place, knew how long she had been in the hospital, and recognized those about her by name. At times she has exhibited some evidences of depression, would cry, state that she had been treated badly by her family, that they were against her, and that she wished to be released so that she might go out and lay herself on the railroad track and be killed. She said that God had told her to go do this. Though giving expression in this manner to possible auditory hallucinations, her condition has not been such that the actual hearing of voices could be verified, and it, therefore, remains questionable whether or not actual hallucinatory experiences have been present. It is suspected that we are dealing not with actual auditory hallucinations in this instance, but rather with an experience similar to that involved when a person speaks of "the voice of conscience." More a matter of looseness of expression than an actual hallucination. Then, in her periods of betterment, when she is more accessible and co-operative, her reactions are in many ways similar to those of a child: she becomes pettish, will pout or coax and perhaps dodge an inquiry concerning some of her past conduct by a smile or laugh. Most of the time she is, however, as you see her today, inaccessible, mute, and resistive, requiring constant attention and waiting upon in every detail of her care.

As you have seen this patient today she certainly presents a psychotic picture very suggestive of dementia præcox. We have the mutism, refusal of food, resistance to passive movement, at times almost amounting to negativism, the inaccessibility, the mental confusion, the cyanosis of the extremities, the possible auditory hallucinations, and the mildly developed per-

secutory ideas. But we have a long history of illness to consider in this case. The onset occurred seven years ago shortly following the establishing of the menstrual function which has always been abnormal in its appearance. Prior to this onset the girl was considered to be nervous and of high-strung temperament, always having her own way with her parents. At the beginning there was evident the motor disturbance of a myoclonic character, and throughout the subsequent course of the disease up until the present time these jerking movements have recurred with exacerbations of her illness. In the early days there occurred episodes of fleeting blindness and aphonia as evident hysteric manifestations. Also, the original examination showed anesthesia of the lower extremities of the stocking type distribution, another hysteric feature. There was no evidence then of organic disease of the central nervous system nor has there been since that time. Following a long period of hospital residence she recovered to such a degree that she could be at home, but during this period also had two "attacks" of a couple of weeks' duration, occurring in connection with menstrual periods, the only two menses in a couple of years' time. These episodes were characterized mostly by the myoclonic disturbance and but little by grossly abnormal mental symptoms of psychotic nature such as have been present in this last attack in which you have seen her.

Now the question arises as to whether we are to consider this last episode by itself as a purely catatonic manifestation of dementia præcox, or are we to consider it in relation to the entire disease history. This case illustrates well the value of studying the entire disease history and not alone an isolated episode in this disease. The past history of this case with the earlier examinations can leave no doubt as to the clearly hysteric nature of the disorder. The fact, too, that through all of this illness there has been demonstrable during her periods of betterment no token of dementia is extremely significant. We can hardly expect a præcox after a course of several years to escape some evident degree of deterioration or emotional leveling. May it not be questionable whether a hysteric may not later



develop a true dementia præcox? This may be a possibility, but it, at best, is not a commonly observed occurrence. Personally I do not recall such an instance, though there are many where the differentiation between the two conditions has been impossible without following the course of the disease for a considerable period. On the other hand, is there anything specific or pathognomonic in such catatonic manifestations as we have seen exhibited by this patient? In many toxic psychoses and in some acute confusional states of other than toxic causation, we not infrequently see catatonic manifestations without the appearance of a true præcox. In other words, again, it is not the isolated symptom which is of final importance so much as it is the setting of this symptom in constellation with others noted during the course of the disease. Possibly we may more safely wait to observe the further course in this case before reaching a final diagnostic opinion, but at all events at the present time a diagnosis of hysteria is better supported than is one of dementia præcox.

The prognosis in this case is far from good. As to the present episode, we may anticipate a recovery, but it is reasonable to assume that this may occur only after a prolonged period. This patient has shown a deeply ingrained, possibly inborn, hysteric make-up, and we cannot look forward to much change in this constitutional groundwork which, in fact, constitutes her normal.

*Second Presentation.*—This patient has shown such remarkable changes since you last saw her six weeks ago that she is brought in again. There is not much of the abnormal to be seen today. To be sure, she is easily upset and trembling, but this is due to the excitement of the occasion and will soon quiet down and disappear. She is smiling and happy, helps the nurses with their duties, talks pleasantly with those about her, and spends much of her time at needle work. She is bright and alert, vivacious, and certainly shows no sign, even the slightest, of deterioration. She eats very well and has gained considerably in weight, complains of no weakness, and the jerking movements have entirely disappeared. It is of interest, also, to note



that five weeks ago she had a normal menstrual period and a second one, at the regular interval, last week. These were not associated with any disturbance, either physical or mental. It should be mentioned that she has received daily intramuscular injections of ovarian substance for some ten weeks past. According to relatives, she is now in better health than for many years past.

On the day when you previously saw this patient she was transferred from that hospital to a public institution because of financial stress. There, instead of being in a private room, waited upon for every want, she was placed in a ward room with several other patients and not given so much individual attention as formerly. The nurses were instructed to ignore any unnecessary requests for service and to impress upon the patient that she must help herself. She began to clear up on the fourth day after her admission and within another week was much as you have seen her today, though her condition, especially physically, has continued to improve gradually. Incidentally there is a period of complete amnesia dating from about her last birthday (August) until she, as she expresses it, came to herself in the public institution. She can recall absolutely nothing of what transpired during that interval. There is no question that too much "service" may be given to a hysteric. This girl has been waited upon, petted, and "spoiled" all of her life. Rubbing elbows in a ward of a public institution with some of the elements with which she has not been accustomed has unquestionably served to jolt and loosen some of her mental habits to a degree that there could be an awakening and replacement with more normal trends. Our diagnosis of hysteria has been justified by the outcome in this case. The rather abrupt recovery at so early a date was not anticipated, but this case goes to show that such a reaction is possible. Again, we must emphasize that it is not the one isolated phase of the disease, but rather the course, which is of the greatest value to a correct understanding of the underlying processes, a knowledge of which is prerequisite to a correct diagnosis and rational management of the case.

In conclusion, we may call attention to the fact that the 5 patients which have been presented to you are not at all unusual because of rarity. They represent rather a selection of the common run of cases with which the practitioner comes into contact during the day's work. It is only necessary to point out that all of these first came into the hands of the internist or surgeon. They illustrate the various points of relationship existing between the surgeon, internist, and psychiatrist. In the first patient only do we find a physical disease of medical and surgical, as well as psychiatric interest, namely, hyperthyroidism. There is one feature which is very evident and common to all 5, the signs and symptoms of endocrinic disorder. This element is primarily of medical interest, but we may bear in mind the possible etiologic rôle which this disorder may bear to the mental abnormality, though we have not the opportunity on this occasion to discuss this feature more fully. Each one of these patients illustrates well the point that we must consider the sick individual as a personality and view the entire situation from this broader and more individualistic angle, and not merely as a case presenting symptoms or signs of disease of this or that one system which may be by custom relegated to the care of the surgeon, the internist, or other specialist. We cannot, in other words, safely consider the system disease, whether it be surgical or medical, apart from the individual as a whole.

## CLINIC OF DR. JOHN L. TIERNEY<sup>1</sup>

ST. JOHN'S HOSPITAL

### HEADACHE

**Classification: I. Intracranial:** (a) Cortical; (b) Dural. Consideration of Pressure. Migraine, Type Case, Relation to the Vegetative Nervous System and the Endocrines. Treatment of Migraine. Pituitary Headache, Type Cases, Therapy.

**II. Extracranial:** (A) Osseous; (B) Ocular; (C) Dental; (D) Nasal: (1) Sinusitis (Suppurative), (2) "Vacuum" Headache, (3) Nasal (Meckel's) Ganglion Neurosis, (4) Hyperplastic Sphenoiditis; (E) Neuralgia; (F) Indurative Headache.

HEADACHE, the topic I have selected for today's clinical presentation, is in no sense to be dignified as a disease entity, but must be considered purely as a symptom; however, a symptom so common in ordinary practice and often so outstanding in a syndrome that it deserves special consideration. It is frequently of major importance and the particular complaint for which the patient seeks relief, and one that should stimulate us to a painstaking search for the causative factor instead of a feeble therapeutic attempt to abate pain. The causes of headache are legion and the classifications numerous, most of them haphazard and of very little value in rendering us data of etiologic importance. Probably one of the most tenable, at least one of the most simple and comprehensive classifications I have encountered, is one which divides headache into intracranial and extracranial. Under intracranial, consideration is given to cortical and to dural causes. Naturally the cortex, itself being perfectly insensible to pain, at least to the best of our experimental knowledge, needs little consideration. Of greater importance is the dura. The inner lining of the skull is abundantly

<sup>1</sup>From the Department of Medicine, St. Louis University School of Medicine.

supplied by branches of the trigeminal and other cranial nerves and, like the periosteum, is definitely pain sensitive. These nerve endings are subject to two important affections, pressure, and inflammation, either of which will naturally produce the symptom headache. Pressure, as may be readily understood, comes about in a great variety of ways, through cerebral edema, hyperemia associated with any toxemia of metabolic (nephritis, acidosis), acute infectious (typhoid, malarial), or drug origin (alcohol, tobacco), tumors, hemorrhages, abscesses, etc. Inflammation may affect the dura in association with any of the ordinary inflammatory diseases of the meninges, primarily or secondarily from foci elsewhere. Pressure seems to be a more important consideration, and we frequently note in states where both inflammation and pressure are associated, definite clinical improvement by the relief of the pressure alone, such as the clinical benefit, including relief of headache, following lumbar puncture in meningitis. The beneficial effect of pressure relief is also seen in decompression in the case of various types of brain tumor.

The second great subdivision, or extracranial, includes diseases of the cranial bones themselves and reflex headache arising from ocular, dental, and nasal disturbance, various neuralgias, such as trigeminal, those arising from vertebral diseases and the indurative or so-called rheumatic headaches arising from inflammation of the muscular aponeurosis of the occipitofrontalis, and such interesting reflex headaches as are frequently found associated with apical pulmonary lesions, etc.

Our attempt shall be to present a few selected cases under both great subdivisions, and under the first heading the most outstanding type is migraine. We find many contentions, some of them apparently biased; for instance, such statements that most cases of migraine are due to ocular disturbances or nasal pathology. For instance, one observer makes the statement that a great majority of headaches of whatever time standing and diagnosed as migraine, that are met with in the general practice of medicine are sphenoidal in origin. There is a saving grace in the phrase "diagnosed as migraine," because it is our

firm belief that true migraine is most definitely an entity and due neither to ocular nor to nasal pathology. How many cases consult the internist or neurologist who have run the gamut of competent nasal and ocular investigation and therapy without relief. It has been truly said that migraine is philosophically interesting, though therapeutically pride breaking, a neurosis indicating family instability, almost always occurring in families of which other members have some nervous or mental disorder or are brilliantly able. It is assuredly a disease of which headache is but one symptom. We, personally, despite the contention of the oculist, the otorhinolaryngologist, and the gastroenterologist, with his mind focused on the gall-bladder, believe that migraine is an entity based upon a vegetative nervous system disturbance and more fundamentally upon an endocrine imbalance. We refer naturally to true migraine, realizing that the diagnosis of migraine is frequently erroneously made in the presence of paroxysmal unilateral headache due to a varied etiology.

Before proceeding to a discussion of the etiology of migraine and the presentation of an interesting case from the standpoint of therapeutic result, permit me to briefly express our clinical concept of migraine. It is a disease of attacks, periodical, occurring every week, month, and in exceptional cases every year. There may be an initial period of depression or of intellectual hyperactivity, and within twelve or fourteen hours the second period, that of headache, appears with a sensation of pressure in the orbital, supra-orbital, or temporal region followed by actual pain, which becomes diffuse, not limited to nerve distribution and not extending to the suborbital area. As Dieulafoy says, the pain may be unbearable, likened to the crushing, perforation, or dislocation of the bones of the skull, often increased by walking and by movement. The face is pale or injected, the temporal arteries on the affected side frequently are hard and prominent, the blood-vessels of the retina are dilated, and there may be hyperacusis and photophobia. The pain may shift suddenly from one side to the other, there is nausea and vomiting, occasionally abdominal pain which leads to confusion in diag-

nosis. There may or may not be ophthalmic symptoms. If present, the usual manifestations are a monocular or binocular hemianopia and scotomata of various types, floating specks, flashing balls of fire, stars, or the typical fortification figures. Transient aphasias, paresthesias, and even epileptiform convulsions have been associated; in fact, there is throughout an analogy between migrainous attacks and minor epilepsy.

The etiology independently of ocular, nasal, or gall-bladder disease covers a wide range and in many respects is interesting. The older authors felt that it was associated with a gouty diathesis and Trousseau remarked that an individual who in his youth suffers from migraine will later be liable to eczema, asthma, gravel or gout, a most interesting remark because of the fact that any of these particular manifestations may have a vegetative nervous or an endocrine relationship. Rheumatism and chorea at times seem to be related. In migraine there are no demonstrable histologic changes, but the symptomatology clearly suggests disturbed function of the cerebral cortex supported by the usual sensory disturbances and the frequently associated aphasia. Spitzer has suggested abnormal narrowness of the foramen of Monro, which when the brain becomes hyperemic becomes temporarily occluded, producing increased pressure in the ventricles and headache. Levi feels the disease arises in the medulla, and neuralgia of the meningeal branches of trifacial has been considered. A prominent theory in the causation of migraine is disease of the sympathetic nerves producing vasomotor disturbance. DuBois Raymond considered it an excitation, and Mollendorf, a paralysis of the sympathetic nerves, opposing views which have led to the description of two forms of hemicrania—hemicrania sympatheticonia and hemicrania sympathetoparalytica. The clinical facts seem to support the vasomotor concept of the disease. The usual visual and sensory disturbances, auræ, aphasia, chilliness, pallor followed by flushing, perspiration, temporal vessel constriction, retinal vascular changes, slowed pulse, are all suggestive of vasomotor phenomena, and the headache could be easily explained by the increased intracranial pressure produced by dilatation of the cere-

bral arteries. The transient character of the focal symptoms, such as the visual changes, the paralysis, etc., suggest vasomotor phenomena. Against this conception is the fact that in many cases of true migraine there are no demonstrable vasomotor phenomena.

Therapeutic attempts have been legion and almost every variety of treatment recommended. Refractive errors have been corrected, sinuses drained, occupations changed, constitutional states corrected, and gall-bladder drainage, surgical and non-surgical, and colonic irrigation recommended, carbohydrate, protein-free diets instituted, and a variety of drugs including alkalies, bromids, morphin, cannabis indica, caffein citrate, strychnin, pilocarpin, ergot, antipyrin, phenacetin, aspirin, pyramidon, and more recently peptone and various calcium preparations have been exhibited with variable results.

It strikes us that there are some features about migraine which force us to consider its relationship with the endocrines, notably such clinical facts that the attacks in women occur more frequently associated with the menses, and usually no matter how severe the disease may be, cease with the menopause, although there have been in our experience notable exceptions to this rule. Other interesting features have occurred in a number of cases, namely, the complete freedom from attacks during pregnancy and the coincidence of polyuria and bradycardia with attacks. J. Herbert Fisher, of the Royal London Ophthalmic Hospital, himself a sufferer, describes the migraine spectrum as symmetric, represented by scotomata, expanding from a central point or first appearing in the temporal periphery of the fields or affecting homonymous halves of the fields. He thinks that the lowly organized spectra of migraine could be produced by irritation of the visual nerve-fibers at the base of the brain; at the chiasma the expanding central scotoma and bitemporal scotoma; at the optic tract the homonymous scotoma. He feels that the periodic temporary swelling accompanying a functional overactivity of the pituitary body explains migraine better than any other hypothesis. Of course there is considerable basis for this contention, but at the same time there is a most



definite paradox, namely, the freedom from attacks during pregnancy, a time when ordinarily according to Erdheim and Stumme there is a definite enlargement of the pituitary and probably an overfunction as exemplified in the occasional clinical presentation of acute acromegalia during pregnancy which subsides with the termination of same, and, furthermore, migrainous phenomena do not usually occur in the course of pituitary tumor.

There is undoubtedly still much confusion in our interpretation of pituitary states as exemplified in the fact that for many years we did not realize that an individual might present the gross clinical characteristics of a previously existing hyperpituitarism, and at the time of observation really be in a transposed state of physiologic hypo-activity. For example, a case of preadolescent hyperactivity of the anterior lobe of the pituitary resulting in gigantism quickly goes over into a state of hypo-activity retaining the physical characteristics of gigantism as representative of his previous hyperactivity, but at the time of observation presents a loss of skeletal muscle tone, physical weakness, loss of libido, etc., as evidence of his deficiency, a condition actually requiring pituitary substitution. This frequent clinical occurrence explains the apparently paradoxically beneficial effects of pituitary therapy in some states of gigantism and acromegalia which are unquestionably indicative of quondam hyperactive, but present hypo-active pituitary states. While admitting the frequent clinical occurrence of migraine in individuals of pituitary make-up, and in a considerable number of cases the amelioration of symptoms under pituitary treatment, we cannot wholly admit a disturbed pituitary as the sole causative factor. We do, however, feel that the disease is one due to endocrine imbalance, and if we assume the vasomotor conception of migraine the contention is more convincing, because we recognize more clearly each day the association of perverted sympathetic states with disturbed endocrine function and abnormal vasomotor phenomena associated with disturbed adrenal, thyroid, ovarian, and pituitary states.

There have been attempts to differentiate migraine and pituitary headache, and while feeling that migraine is associated



with endocrine, at times pituitary, disturbance, we do feel that there is a special and separate type of headache distinct from migraine which seems to be an entity and which has been termed "pituitary headache" and described in the literature by Pardee, Blumgarten, Engelbach and the author, and a number of other observers. There are many differential features described by many men, but in most attempts at a differential diagnosis, which at best are conjectural, very little consideration is given to the fact that the pituitary through its vegetative nervous and vasomotor influence may also be a factor in the production of migraine. The most outstanding differential point is the paroxysmal one. In our experience true migraine has been most distinctly paroxysmal, has been usually hemicranial, has been constitutional, hereditary, and ordinarily associated with visual disturbance, nausea, and vomiting, and commonly our cases of pituitary headache have been more found in individuals with other signs of pituitary disturbance, have been bilateral, non-paroxysmal, associated with different ocular manifestations, if any, and not usually accompanied by nausea and vomiting. However, despite the confusion that still exists in the differentiation of these types we feel that the facts presented open up, at least, interesting lines of speculation, and we will present today cases demonstrating what we believe to be definite exemplification of both types. We may say in passing that both types conform to the first great subdivision, namely, that of intracranial headache.

**Case I.**—The first case for presentation today is a young lady of twenty-nine years, coming under observation with two outstanding complaints, first, an undue fatigability, and second, headache, periodical, paroxysmal, usually hemicranial, either right or left, originating behind the eye and radiating to the occipital region. This is associated with extreme nausea and vomiting, complete prostration with incapacity for from two to four days. They usually occur around the menstrual time, but seem upon other occasions to be precipitated by excitement, irregular hours, indiscretion in diet, constipation, travel upon

the train, etc. These attacks began at the age of six years and for the past twenty-three years have gradually grown in frequency and in severity until in the past year they have occurred as frequently as twice a week, the usual exciting features being those mentioned above, although the common tendency is occurrence about the menstrual time. Menses began at sixteen, regular, normal flow and duration. There is nothing of significance in the past history or anything of psychopathic interest in the ascendancy. The outstanding complaint is headache, for which the patient seeks relief. The physical examination shows a tall slender girl of the type usually termed eunuchoid, the hands and feet are cool and moist, color is generally good, the head is entirely negative except for slight pressure tenderness over the frontal sinuses. The ears are normal, in-

<i>Adrenalin Test.</i>				<i>Remarks.</i>
Time.	Pulse.	Respira- tion.	Blood- pressure.	
1.25	84	24	98/62	Patient feels O. K. and normal, somewhat sleepy.
1.27	84	24	98/64	Injected ss c.c. of adrenalin.
1.30	84	22	100/62	
<i>After Injection</i>				
1.32	84	24	98/62	Tingling sensation all over. Patient more conscious of heart beat.
1.34	72	16	100/62	Palpitation of peripheral blood-vessels.
1.36	90	20	106/68	Extremities cold.
1.38	84	20	108/62	
1.40	84	20	108/62	
1.42	84	20	112/72	
1.45	80	18	110/70	Patient conscious of heart beat. Pulsation in epigastrium, arm, and neck.
1.50	80	18	114/60	Extremities are cold. Feels like electric shock all over body.
1.55	80	18	114/60	Marked tremor. Palpitation of heart, hands and feet cold.
2.00	92	18	122/74	Back dry.
2.05	78	16	116/60	Chest and abdomen dry.
2.10	84	16	112/60	
2.15	84	20	112/68	
2.20	88	20	118/64	
2.25	84	18	118/70	Patient feeling better. Heart pulsation marked, neck and epigastric less.
2.35	84	18	112/70	Patient feels normal, still slight palpitation of heart.
2.40	84	18	110/64	Tremor slight. Body surface dry,
2.45	85	20	108/74	feet cold. Patient feels about normal.
2.55	88	16	108/74	
3.05	80	20	104/64	
3.15	84	16	102/68	

## HEADACHE

1523

<i>Atropin Test.</i>				<i>Remarks.</i>
Time.	Pulse.	Respira- tion.	Blood- pressure.	
1.40	88	20	108/72	Patient feels fine, no headache.
1.45	88	20	108/72	Injection of 1/150 atropin.
After Injection				
1.47	80	24	100/78	Mouth feels dry. Eyes seem to be dilated
1.49	84	24	104/72	somewhat. Extremities moist. Hands
1.51	80	22	110/74	and feet moist. Peripheral pulsation in
1.53	80	22	110/74	neck. Hands and extremities not so
1.55	84	20	110/76	moist. Abdomen, chest, face, and fore-
1.57	80	18	106/74	head dry. Mouth dry, eyelids feel tired.
2.02	80	18	104/74	Mouth and lips dry. Tongue sticky.
2.07	80	18	98/70	Abdomen and mouth moist.
2.12	84	18	98/72	
2.17	72	20	96/72	Throat, mouth, lips dry.
2.22	70	20	96/72	
2.27	78	18	96/70	
2.32	80	18	98/76	Lips becoming moist, eyes dilated.
2.35	78	20	96/70	Palms and soles moist and feet cold.
2.37	80	18	98/76	
2.42	73	18	98/72	
2.47	74	20	100/68	
2.52	70	18	98/68	
2.57	74	18	100/70	
3.02	70	18	100/70	
3.12	72	18	98/74	Mouth dry. Back wet, palms and soles
3.22	70	18	98/70	moist, lips getting moist.
3.33	74	20	98/72	

<i>Pilocarpin Test.</i>				<i>Remarks.</i>
Time.	Pulse.	Respira- tion.	Blood- pressure.	
2.30	80	20	108/86	Patient in good spirits.
2.36	80	20	100/64	
After Injection				
2.37	86	20	92/60	Face flushed.
2.39	88	18	98/64	
2.41	80	18	108/58	
2.43	86	18	102/60	Lips dry, hands moist, no other sensory
2.45	86	18	102/60	disturbances.
2.50	80	20	98/68	Patient has carotid pulsation.
2.55	80	20	92/66	Lips still dry, hands and feet moist.
3.00	82	18	102/72	
3.05	82	20	102/72	
3.10	80	20	108/70	No change of feeling. No sensory dis-
3.15	80	20	108/70	turbance of any kind.
3.20	80	20	108/70	
3.25	82	20	102/76	
3.35	80	20	104/72	

cluding air and bone conduction. Eyes show a slight pupillary inequality, reactions and muscle movements are normal with no thyroid signs. The nose, mouth, and pharynx are normal except for a slight tonsillary hypertrophy without evidence of infection. The thyroid is palpable and there are a few small hard, discrete glands in the posterior cervical chains. The chest shows a slight increase in tactile fremitus in the right upper part without other abnormality. The heart is negative except for a faint systolic roughening at the apex and in the pulmonic area, which disappears completely on deep inspiration. The pulse is slow and otherwise normal. The abdomen and intra-abdominal viscera are perfectly normal except that a spastic sigmoid is palpated without tenderness. The pelvis is negative. Neurologic examination shows no sensory disturbance. Babinski, Chaddock, Gordon, and Oppenheim negative. Achilles and patellars active and equal, abdominals present and equal, and but one striking abnormality was noted, and that, the *presence* of a *very positive Chvostek*, although Trousseau's and Hoffman's signs were negative and there was no other clinical history or physical evidence of a tendency to tetany. The patient was placed in the hospital for more intensive study to determine a possible causation of her outstanding complaint—headache.

Laboratory: Single specimen of urine totally negative except for a faint trace of albumin. Twenty-four-hour specimen, amount 1500 c.c., specific gravity 1012, faint trace of albumin, otherwise totally negative. Blood: Leukocyte count 7400, hemoglobin 80 per cent., erythrocytes 5,200,000. Differential count: Lymphocytes 31 per cent., polymorphonuclear leukocytes 66 per cent., and transitionals 3 per cent., creatinin 3.3 mg. per 100 c.c. Uric acid, 3.8 milligrams per 100 c.c. Non-protein nitrogen: 21 mgm. per 100 c.c. Wassermann negative. Sugar tolerance: First specimen .095 per cent., after fifteen hours' fast. Second specimen one hour after the ingestion of 1.59 grams dextrose per kilogram of body weight, .133 per cent.; third specimen, two hours after ingestion of dextrose, .138 per cent. The basal metabolic rate (Benedict's portable) minus 17 per cent.

Radiograms of the skull taken for the nasal accessory sinuses showed a very slight cloudiness of the right ethmoid, a finding not verified by other observations. There was no doubt in our minds that the diagnosis in this case was a true migraine, and the collateral clinical determinations showed a number of features of some significance, notably a definitely lowered basal metabolic rate with an adrenalin test not in conformity, an apparent cloudiness of one ethmoid not verified by physical examination, and the most interesting feature of a very decidedly positive Chvostek phenomenon Number 3, which is presumably pathognomonic of tetany. Our clinical experience, despite the literature, has taught us that Chvostek sign Numbers 1 and 2 are frequently positive in the absence of other signs of tetany, but rarely have we found a complete Chvostek such as was manifest in this case without other clinical signs of tetany. This peculiar association gave rise to a most interesting train of reasoning. In the first place, a full Chvostek sign is considered as pathognomonic of tetany which, in turn, is deemed due to parathyroid disturbance with calcium deficiency; and calcium is of undoubted therapeutic value in tetany. Second, epilepsy which, as we have seen, seems to be allied with migraine has been suggested as being of parathyroid etiology and favorable results have been obtained in epilepsy by using parathyroid medication by Vassalle, Parhon and Golstein, and Claude, Schmieregeld and Schmorl have found at autopsies of epileptics numerous appreciable lesions of the parathyroids; and third, Schlesinger and others empirically found beneficial results in the treatment of migraine by the administration of calcium. Alfred Schlesinger (Schweig. med. Wchnschr., Basel, 53, 77, January 25, 1923) assumes migraine to be an intoxication as a result of poor dissimilation. He gave calcium glycerophosphate 15 cg., ferriprotoxalat oxydulat and ext. gentinæ aa cg. 10. He felt that this treatment like peptone brought about hemoclastic shock. Out of 19 cases, some showed a pronounced improvement, and 9 an immediate, permanent, and complete recovery. He asserts that the important component is the calcium glycerophosphate. Following this peculiar line of deductive reasoning and interested

in the reported success of Schlesinger, we advised calcium therapy, deliberately neglecting such an outstanding feature as the definitely lowered basal metabolic rate. We may say parenthetically that since the determination of the basal metabolic rate has become clinically feasible we have routinely made same with great value. However, in cases I cannot elucidate now we have frequently neglected the basal metabolic readings and fallen back upon disreputable clinical evidence with therapeutic success. We are cautioned about accuracy and are given undue ranges of normality such as +10 and -10 and even +20 and -20. Why this equality up and down I cannot comprehend. Considering variables as I see them, I might neglect a +30 reading, but might attach significance to a -8 basal metabolic rate. Anyway the case under discussion was sent back to the attending physician with the recommendation that first of all a diligent trial of straight calcium therapy should be instituted, and if unsuccessful at a later date to consider a treatment based upon the lowered basal metabolic rate or the empirical use of such a preparation as peptone which has in the hands of Widal and other observers proved therapeutically successful. This patient was seen about August 1st. From August 4th to 8th, following rather a strenuous time, coincident with the menstrual period and following a long train journey, the patient had a severe typical attack of headache, which produced incapacity for thirty-six hours. On August 20th the administration of calcium in the form of calcium glycerophosphate, gr. x t. i. d., was begun, without additional treatment except that advice was given concerning the regulation of the bowels and general forced feeding. Sixteen weeks have elapsed since the administration of the treatment and no severe headaches have been experienced in that time, although it will be recalled from the history that in the past year these severe migrainous headaches have occurred on an average of twice a week. This and similar therapeutic results may be distinctly a *post hoc ergo propter hoc* argument, but we present this type case as one which appeals to us as of outstanding interest and which should suggest to you as students a consideration of the *possible relationship* of true migraine with

the sympathetic and parasympathetic nervous systems, with the endocrines, not only the pituitary but the parathyroid and other glands; metabolic aspects in general and the importance of calcium and other drugs which affect the vegetative nervous system. It may be remarked in passing that Widal and his school consider migraine an anaphylactic phenomenon and that calcium in various forms, such as calcium chlorid or lactate, by mouth, and afenil, a chlorcalcium carbamid, for intravenous use, have been found therapeutically efficacious not only in tetany, but in many cases of frank anaphylactic presentation such as urticaria, asthma, serum disease, hay-fever, and angioneurotic edema. Even if migraine is an anaphylactic state we must still look to the vasomotor system, the sympathetic and parasympathetic, the body metabolism especially of such salts as calcium and potassium (remembering that calcium is a cellular element essential to sympathetic stimulation and potassium to parasympathetic stimulation), and behind all of this to the endocrines.

You may have noted some interesting paradoxes. Migraine if due to a vegetative nervous mechanism, judging from its ordinarily associated vasomotor phenomena, at least in its prodromata, seems to be a hyperactive sympathetic state, and if calcium produces stimulation of the sympathetic, it should intensify rather than relieve migraine. But we must remember that while sympatheticotonic symptoms may predominate at first, the real attack in most cases, including the headache, is probably due to dilatation of the cerebral arteries with increased intracranial pressure, which suggests a hyperparasympathetic or at least a sympathetico-paralytic state. The dilatation of the retinal arteries on the affected side is similarly suggestive. Probably this same clinical conflict has given rise to the German concept of a hemicrania sympatheticona and a hemicrania sympathetico-paralytica. Remember that the sympathetic and parasympathetic are antagonistic in their action and that the prodromal sympathetic symptomatology of migraine may be a compensatory attempt to combat the perversely overactive parasympathetic, and failing in this the para-



sympathetic triumphs and a vasomotor dilatation with increased intracranial pressure and headache results. This suggests the possible beneficial action of calcium through the sympathetic in the relief of migraine and may give rise to some interesting speculation concerning the genesis of a seemingly allied condition—epilepsy. There has just come to my desk an article by Dr. F. M. Pottenger of Monrovia, California, "The Relationship of the Ion Content of the Cell to the Symptoms of Disease with Special Reference to Calcium and Its Therapeutic Application," *Annals of Clinical Medicine*, vol. xi, 3, 187. Pottenger is a clinician par excellence, but one who thinks along physiologic lines, and his views concerning the vegetative system are illuminating. He states that he has used calcium sufficiently to demonstrate its influence in practically all parasympathetic syndromes. He mentions the relationship of protein foods to calcium and states that protein foods are broken down into certain acids which combine with calcium and cause its rapid elimination. He feels that the reason why patients suffering from asthma and eczema and other diseases of this type do best on a low protein diet is now furnished with a physiologic explanation. He mentions his method of administration, a 5 per cent. solution of calcium chlorid, 5 to 10 c.c. intravenously at varying intervals. This is given very slowly and is often followed by a sensation of warmth or heat similar to that experienced after *afenil* heretofore mentioned. We have digressed somewhat, but we trust with value. You are students and should be impressed with the relationship of the vegetative nervous system to clinical symptomatology and a field of therapy is opened, which for fundamental data I would refer you to Sollmann's "Pharmacology of the Autonomic System," *Physiological Reviews*, vol. ii, No. 4, 479, October, 1922.

The second case which we will present conforms to our concept of true pituitary headache of the functional type, that is, headache in an individual presenting other signs of pituitary disease, but with no evidence of pituitary tumor and relieved by the administration of pituitary extract. The ordinary explanation of this headache is the compensatory attempt of the pit-



uitary to make up for deficiency by a physiologic hypertrophy of the gland in a small sella turcica. The beneficial effect of the administration of pituitary extract is on the basis that these extracts supply a substance which removes the demand or the need for physiologic and compensatory hypertrophy.

**Case II.**—Mr. L. C., aged twenty-four. Chief complaints: Severe headache usually bitemporal, sometimes more severe on one side than the other, localized as a rule in an area about the size of a half-dollar in the temporal region, penetrating deep into the head without particular radiation to the front or back, with a marked hyperalgesia over the temples. There seems to be a retro-ocular pressure causing the eyes to feel as if they were bulging out and every step or quick movement makes the pain almost unbearable. There has never been nausea and vomiting and scotomata have been but seldom present, and then in the form of small floating specks of black and white. There is an associated fatigability and lack of energy, a definite tendency to nocturnal polyuria with urgency, a frequently increased output, but no definite polydipsia or polyphagia. There have been no particular weight or dermal changes.

The patient being a student of medicine has a definite insight into the symptomatology and we quote from his own description:

"There was no definite sudden onset of the headache, but as well as can be recalled they began about four years ago. From the beginning the headaches have been located in both temporal regions, sometimes more severe on one side than on the other. The frequency at first was about every seven days, lasting from one to two days, always present in the morning upon arising and of about the same intensity throughout the period. This condition was not given much attention at this time and remained about the same for a period of one year. During this first year my eyes were refracted and a +1 lens was prescribed for both eyes, the object of the refraction being to relieve the headaches. The lenses were worn constantly for a little more than a year without any relief; in fact, the headaches became

more severe and increased in frequency. I then had my nose and sinuses examined, the examination proving negative.

"At approximately the second year I was having the headaches on an average of twice a week, so severe at times that I was unable to study and do my work as I had been accustomed to doing. The pain seemed to be getting deeper, yet the skin over the temples was tender. There seemed to be a pressure behind my eyes causing them to feel as if they were bulging out, and with every step and quick movement the pain was almost unbearable. During this time I became an aspirin addict, sometimes consuming as much as 60 to 70 grains in twenty-four hours, which amount relieved me only slightly, if at all. I have taken many kinds of headache tablets, some of unknown composition, and all of them without relief. For instance, the ordinary migraine tablet that gave so many of my friends relief seemed to have no effect on me even in much larger doses than they were taking. Cold and hot applications to the head and pressure upon the temples had no effect.

"After several months of the above condition, I noticed that between attacks, unlike I had been before, I did not have the desire or 'pep' to double up on my work as I had been doing to accomplish that which had been neglected during the attacks. I noticed that by the time I arrived home from school I was tired and that by 8.30 or 9 P. M. I was 'all in,' whereas I had been accustomed to working until 11 or 12 P. M. It seemed as though I was getting lazy, but I was unable to 'pep up.' I made every effort to conceal my fatigue during the day at least. With this fatigue the headaches were becoming more frequent and more severe, sometimes lasting nearly a week, with then an intermission of a few days. All of my life I have been bothered with a nocturnal polyuria, necessitating arising several times during the night; in fact, never prior to this time had I experienced a night without interruption. This condition was gradually becoming worse, necessitating my arising from five to eight times in a night. For this trouble I was cystoscoped, an unusually small bladder reported, and treatment was directed toward enlarging it, which treatment consisted in repeated cystoscopic

operations introducing gradually increasing amounts of water. This treatment gave me no relief, either from the nocturnal polyuria or the very frequent urgent desire to urinate, nor was I relieved of my inability to retain urine for any considerable length of time. I was repeatedly cystoscoped and treated locally with silver nitrate without relief.

"By approximately the fourth year I was experiencing the headaches almost constantly, and they were more severe than during the preceding years. They were bitemporal, at times very penetrating from side to side, not radiating in any other direction. The pain was so severe that I was incapacitated to a considerable extent. There was a marked scotoma in the form of white and black spots, no vertigo, vomiting, or nausea. Pain was not relieved by anything that I could do. I was unable to turn out the character of work I desired, was always abnormally tired: for instance, an extra trip down town or anything out of the ordinary routine fatigued me to such an extent that I required bed rest. My capacity was definitely limited. I could sleep most any time, even with a rather severe headache, because I was always very tired. I required calling several times in the morning and had to be virtually dragged out of bed. Upon awakening I felt as if I had not had half enough sleep, felt very heavy and dull; every morning was the same old story (I had my headache). The polyuria had not improved from the previously described state."

The past history was rather insignificant except for measles and mumps. Venereal history negative, personal habits regular, tea, coffee, tobacco, and alcohol in moderation. Patient has been married for one year, wife has had no pregnancy. Family history is insignificant except for a migraine in mother. The physical examination shows a definite pituitary type of individual, measurement from the symphysis to the soles of the feet practically equal to those from the symphysis to the vertex. Hands are suggestively pituitary, the jaw is slightly prognathous, supraciliary ridges prominent, and there is a slightly increased amount of hair. The head shows no gross abnormality except marked bitemporal tenderness. Ears, eyes, nose, and throat

are negative, thyroid is not palpable. Chest, heart, and lungs entirely negative, abdomen, including intra-abdominal viscera, negative. Neurologic examination negative throughout. The routine laboratory examinations including the Wassermann were totally negative. The stereoscopic x-ray examination of the skull showed the sella turcica practically normal in size. The posterior clinoid process was rather long and curved forward until it touched the tip of the anterior clinoid process producing the picture of the so-called shut-in type of sella. As mentioned above, routine ocular and nasal examinations were entirely negative. The make-up of the individual, the character of the headache associated with the muscular fatigability, mental retardation, decreased libido, a tendency to polyuria, the character of the sella turcica, and the absence of other factors in the production of headache led us to the conclusion that we were dealing with a true case of pituitary headache. On April 30th of this year the patient was placed upon the anterior lobe pituitary substance, gr. v t. i. d., and antuitrin, the anterior lobe extract, of Parke-Davis & Co., 1 c.c. hypodermically twice weekly. The next observation was made twelve days later, and we quote from our notes: "General condition has definitely improved; states that he feels better than he has in two years." The patient has been on treatment rather consistently since that time and has been under periodic observation. Because of the fact that being a medical student he has a good insight into the condition, I am going to permit him to resume the story of his therapeutic advance:

"Since I started the present treatment about six months ago, I have experienced a very rapid improvement in all symptoms described above. Beginning with my first day of medication I experienced a period of two weeks without headache. Immediately following this time I had an atypical headache which lasted for one day. I at first attributed my lessened fatigue to the fact that I was relieved from headache, but as time went on I noted that I was becoming more alert, more interested in my work, and my capacity was increasing from week to week. In fact, all of the symptoms from which I had

been suffering had within a month's time disappeared. Particularly did I notice less fatigue, since within two months after medication was started I started to do heavy manual labor and worked hard for three months, holding up very well. I experienced no headache and apparently was no more fatigued than my fellow workmen. During this period I noticed that I was not forced to get up so often during the night to urinate, neither was I experiencing the frequent and urgent calls during the day, my sexual desire was increasing, and intercourse gave me more pleasure. During the last two months there was such a marked improvement in all symptoms that I would forget treatment for as many as four or five days, at which time I would begin to notice an unusual fatigue, although my routine work from day to day remained the same. There was, however, during these periods no return of the headache, only fatigue was noticeable. Upon resuming medication I would notice within from twelve to twenty-four hours a disappearance of the fatigue and a return to normal.

"Being now on very regular treatment, I have no headache of any type, no scotomata, no abnormal fatigue, and experience a definitely increased capacity both mental and physical, and an increased libido sexualis. I am able to retain urine for much longer periods of time, being practically normal in that respect, and I have nights in which there is no interruption, although I still frequently have a nocturia of two or three times."

We feel that this represents a true pituitary headache, and it is significant to note in addition to the relief of headache the improvement in the polyuria, the increased libido, accelerated cerebation, the decreased fatigability and increased skeletal muscular power, all features, which according to our classification of pituitary functions, come within the province of the anterior lobe except the polyuria, which is usually attributed to decreased function of the pars intermedia. Furthermore, the tendency to relapse when treatment was neglected, and the improvement after resumption of same, increases our conviction.

This third case we feel represents a type of pituitary headache closely resembling migraine.

**Case III.**—Mrs. J. S. Referred by Dr. Edward Higbee, St. Louis.<sup>1</sup> Chief complaints: Terrific attacks of pain about the eyes and temporal regions associated with dimness of vision, swelling of the peri-ocular tissue, associated with nausea and vomiting. Usually coming on immediately preceding or following the menstrual period, associated with constipation, distention of the abdomen, cold hands and feet, rapid loss of hair, and irregular menses. Duration of complaint eleven years, with the onset gradual. These attacks have occurred since the age of fourteen, consisting of terrific pain about the eyes, forehead, with nausea and vomiting, usually associated with the menses, and producing marked prostration for from one to three days. Periods have always been irregular, sometimes occurring as much as ten days early, always scanty, usually one day in duration. Patient has been married ten years with no pregnancy. Eleven years ago first noticed visual defects, at which time eyes were refracted and glasses prescribed which rendered some relief, except that the attacks of terrific ocular pain associated with nausea and vomiting still continued to occur every month. Patient states that during these attacks the eyes were very much swollen, seemed as though they were pushed forward, and unable to close the lids without difficulty, etc. These attacks of pain were so severe that the patient would fall to the floor in paroxysmal agony. Past history unimportant except for head injury in childhood which probably has no particular bearing upon the case. Personal history unimportant, family history likewise insignificant.

Physical examination shows a slender woman with marked pigmentation about the face, eyebrows, neck, and forearm. There is no particular adiposity or abnormal distribution of hair. Hands are rather of the pituitary type, some clubbing of finger tips. Head is negative, ears negative, eyes show a slight pupillary inequality with no irregularity or disturbance of reaction or muscle movement. Nose, mouth, gums, throat negative. Thyroid slightly full; chest, including heart and lungs, negative; abdomen normal throughout. Pelvic examination shows a small

<sup>1</sup> Studied in conjunction with Dr. William Engelbach.

uterus, retroflexed. Reflexes negative except positive Chvostek. Special examination of the eyes by Dr. Higbee shows the eyes closely set in the head, lid apertures small, corneas present a keratoconus of unusual type, the top of the protrusion instead of being in the middle of the cornea is about 3 mm. below the pupillary center and gives the appearance of a pear with the stem end pointing down instead of straight out in front. Pupillary reaction normal and no fundus changes are discernible. The field shows no limitation, vision 20/70 corrected with glasses to 20/50. The urine was negative except for a faint trace of albumin. Blood: leukocytes 6200, erythrocytes 4,500,000, hemoglobin 90 per cent., stained smear normal, Wassermann negative. Skiagraph of the skull showed unusual thickness of the walls, frontal sinuses small, maxillary sphenoid, ethmoidal sinuses appear clear. The sella turcica presents an unusual picture, the posterior clinoid process extends in spiral shape toward the anterior clinoid process leaving a space of approximately 3 mm. Within the sella and apparently occupying the space of the hypophysis, we see a number of areas about 2 mm. in diameter which suggest an accumulation of calcified tissue. In reporting this case to the oculist in April, 1919, our opinion was given as pluriglandular insufficiency with the most important evidence pointing to ovarian and pituitary deficiency. Second, spastic colon. The following treatment was recommended: (1) Corpora lutea, 1 to 2 ampules every three or four days; (2) corpus luteum, gr. v, and anterior lobe pituitary substance, gr. v after meals; (3) tincture belladonna and cotton-seed oil as rectal injection to be retained throughout the night. Of these recommendations, only the second, namely, corpus luteum and anterior lobe pituitary substance by mouth was taken, and with remarkable response. The extremely severe headaches which have been present for so many years and so violent in character as to cause the patient to fall to the floor, entirely disappeared, whereas, all former treatment directed toward the eyes and allied conditions had proved futile. It has not been our fortune to see the patient regularly, but Dr. Higbee has from time to time made ocular observations and states that there has



been no appreciable change in the ocular condition for the past four and a half years. He states that the patient has persisted in the oral medication fairly consistently; in fact, has been forced to do so, because if the medication is discontinued for any length of time there is a return of the extremely severe and prostrating headaches. Upon the resumption of treatment freedom is again experienced. The significant findings in this case are the severe attacks of ocular and temporal pain, the irregular menstrual history, the abnormal and interesting findings about the sella turcica and the clearly cut clinical relief by the administration of the corpus luteum and anterior lobe substance. We feel that this case is unquestionably one of pituitary headache and that more than likely the corpus luteum had very little to do with the therapeutic result, although, of course, this assumption should be controlled by therapeutic experiment.

Other examples of intracranial types of headache, such as the various forms of meningitis, tumors, abscesses, etc., we do not feel need special case exemplification, so we will proceed to a consideration of certain forms of extracranial headache. The common extracranial causes are: (1) Ocular disturbance, including muscular fatigue, errors of refraction, hypertension as glaucoma and inflammation as iritis; (2) dental; (3) nasal, paranasal sinusitis, and sphenopalatine ganglion inflammation; (4) neuralgic irritation of branches of the fifth nerve, etc.; (5) rheumatic or indurative headache affecting the aponeurosis of the occipitofrontalis muscle.

First, ocular: It has been claimed that from 40 to 70 per cent. of all headaches are due to disturbed conditions of the eyes, but in our experience this statement is very much too high. The ordinary pain caused by eye-strain is located in the supra-orbital and the frontal region, coming on in the afternoon or early evening following the use of the eyes in work. This pain usually disappears during the night and recurs again after the eyes have been used for some time. Ocular headaches may be temporal or occipital. The frontal and temporal varieties are usually associated with hyperopic astigmatism or compound hyperopic astigmatism, while occipital headache is fre-



quently due to extra-ocular muscle imbalance. When hyperphoria, exophoria, or esophoria are present, even in a slight degree, intense pain may develop at the skull base, such as the panorama headache following train rides, moving picture shows, etc. The pain of eye-strain is presumed to be due to an irritation of the nucleus of the third nerve as well as the center of the fifth nerve, and does not necessarily follow immediately but may occur later as a cumulative effect. Astigmatism even in a slight degree is a very common cause. The possibility of eye-strain in the production of headache may be realized if we briefly recall the anatomy. Each eye has six muscles externally, and these are supplied by three different cranial nerves; and together the eyes have twelve muscles, some of which are antagonists, others are helpful or increase the action, while still others act only as adjuvants in some positions and as antagonists in other positions. The directions in which the eyes may be moved are numerous and the muscle system of the eyes is extremely complicated, and this whole effect of muscles and nerves is designed primarily to move the eyes so that they may both be directed accurately to the object we wish to see, and that each eye shall receive the image of that object precisely upon the fovea which, as you know, is the most sensitive portion of the retina. One can readily understand that this constant attempt at perfect binocular fixation in the presence of a disturbed function must imply tremendous strain in the attempted automatic correction. Realizing these facts, one might be inclined to accept the statement that a very high percentage of headache is due to ocular disease, were it not for the fact that we so frequently see profound ocular disturbances of various types without headache. It has been asked, What relation has use of the ciliary muscle to the production of headache? Dunn feels that excessive, irregular, possibly spasmodic contractions of the ciliary muscle may originate impulses which reach the medulla and overflow into the vagus centers producing nausea and vomiting and into the vestibular centers producing vertigo. Eye-strain may result in a physiologic high pressure on the retinal terminals, thus bringing about unstable intra-ocular tension and

then reflexly intracranial pressure which may result in headache. The causes of eye-strain are so numerous and their correction so technical that it is not deemed necessary to introduce a particular case in exemplification.

The second heading, or dental, requires little attention except to recall the fact that disease about the upper incisors may occasionally produce frontal headache.

Third, nasal and paranasal: Prefacing our remarks upon this aspect it is well to paraphrase Jobson and recall briefly the nervous anatomy. The ophthalmic and superior maxillary divisions of the trigeminal and the vidian nerve are the nerves of common sensation of the nose and its appendages. Meckel's ganglion is the center of sensory nerve distribution and receives its sensory branches from the superior maxillary division and is joined by a sympathetic branch to the superior cervical sympathetic. Meckel's ganglion lies in the sphenomaxillary fossa, just behind and above the posterior tip of the middle turbinate, and at a variable depth from the surface of the lateral nasal wall. It sends branches to the sphenoidal and ethmoidal air-cells, the periosteum of the orbit, mucosa of all parts of the nose, the roof of the mouth, the soft palate, tonsils, and nasopharynx. It is in close relation to the sphenoid sinus, posterior ethmoid cells, and the maxillary sinus. The anterior part of the nasal cavity is supplied by the anterior ethmoidal branch of the fifth nerve. Consequently, it is necessary to appreciate this anatomy in order to understand headaches having their origin in irritation arising in the various areas of this complex nerve distribution.

Under this heading the simplest variety is the ordinary sinusitis. The accessory nasal sinuses are in direct communication with the nasal passage and being lined by mucous membrane are subject to the same infections. They are, furthermore, in close relationship with the interior of the skull. Headaches arising from the sinuses in most cases are due to inflammation of the sensitive lining and pressure. Retention is the important consideration, of far more consideration than the actual severity of the inflammatory process. A mild inflam-

matory condition with obstruction of the opening producing retention and pressure would be more likely to produce severe headache than an extremely severe suppurative process of the sinus with free drainage. One may understand the relationship of headache with nasal disease when he appreciates the close association of the nerve trunks which pass out at the base of the skull with the accessory sinuses of the nose. These sinuses extend under the anterior and middle fossæ of the skull base often with an extreme thinness of bone between. In the posterior portion of the nose are found the optic, oculomotor, trochlear, abducens, vidian, ophthalmic nerve, and the maxillary distribution of the fifth, all of which are in close relationship to the posterior ethmoid and sphenoid sinuses, and consequently easily affected by diseased states of these chambers. The openings of the sinuses are small and a small amount of inflammatory swelling is sufficient to close their openings, producing retention pressure with consequent headache. Again, these openings are situated in the narrow part of the nose so that moderate deformity prevents sufficient ventilation and favors an inflammatory condition about the opening. This is well exemplified by the opening of the frontal sinus which lies under cover of the middle turbinate which when swollen or hypertrophied or pressed outward produces partial closure of the opening with improper drainage. Infected conditions of the sinuses, of course, constitute the commonest type of nasal headache, and sinus headache has certain outstanding characteristics. When acute it is usually intense and throbbing in character with a sense of external pressure, is usually localized to one area, hence unilateral, intensified by stooping, coughing, and jarring movements. Periodicity is a characteristic of this type of headache; it is usually worse in the morning owing to the fact that the frontal and sphenoidal sinuses in the human drain by gravity in the erect position and tend to fill up during the night, giving rise to the early morning or "sun pain." The pain from frontal sinus involvement is frequently referred to the supra-orbital region associated with tenderness. When the ethmoid and sphenoid are affected it is more difficult to localize the pain,

the sphenoidal usually being referred to the temporal region, the occiput or to the vertex of the head, while pain from the ethmoid is usually referred to the back of the eye or the region of inner canthus. It may often be difficult to differentiate the pain of sinusitis from headache of intracranial origin, and a good diagnostic method outside of examination by a competent rhinologist is the spraying of the mucous membrane by a solution of cocain in oil. If sinusitis is due to blocking of the opening and the accumulation of purulent material causing pressure, cocain frequently shrinks the membranes widening the opening and permitting free drainage, releasing the pressure and producing relief of the headache. This explains the clinical fact that many old sinus cases feel better when they have a "cold in the head," in other words, when their sinuses are draining. Any headache relieved by a cocain spray is suggestively nasal in origin.

In addition to the actual purulent involvement of the sinuses there are other types of nasal headache of great importance. These have been described by Sluder as follows: (1) Closure of the frontal sinus without suppuration; (2) the syndrome of nasal ganglion neurosis, and (3) hyperplastic sphenoiditis. This first type, or the so-called "vacuum headache," due to a closure of the frontal sinuses without suppuration, has been described by Sluder, who attributes its first recognition to Dr. Ewing of St. Louis. The underlying cause is usually a hyperplasia of the structures in the region of the infundibulum and hiatus semilunaris. This may be due to many causes within the nose producing hypertrophy of the middle turbinate which closes the tubular opening of the frontal sinus, the air in the sinus becomes absorbed, and a vacuum is produced resulting in pain. The symptomatology of vacuum headache has been described as follows: An inability to use the eyes for near work because of resultant headache which is not relieved by glasses or eye treatment. This headache is accompanied by tenderness at the upper and inner part of the orbit, at the attachment of the pulley of the superior oblique. The attachment of the muscle pulls on the sensitive floor at this point and causes pain,

there is no evidence of pus in the nose or blindness or changes in the globe. The eye disturbance is in the nature of an asthenopia and treatment consists in establishing patency of the nasofrontal duct.

The next type, sphenopalatine or Meckel's ganglion headache, is comparatively common, to briefly recall that the sphenopalatine ganglion lies covered only by the mucous membrane and a little areolar tissue just behind the middle turbinate. It is intimately connected with the fifth and seventh nerves and the sympathetic, is more superficial than any other ganglion of the body, and markedly exposed to nasal infections. Sluder has described a characteristic headache due to disturbance of his ganglion, the so-called lower half headache, although he mentions that this headache may be due to lesions central to the ganglion, such as suppurative and hyperplastic conditions of the sphenoid producing irritation and inflammation of the nerves supplying this ganglion. If the lesion is in the region of the ganglion, cocainization in this area relieves it, otherwise not.

To quote from Sluder, the lower half headache when complete consists of pain about the eyes, the upper jaw and the teeth, extending to the temple, with earache and pain in the mastoid, emphasized at a point 5 cm. behind it. This point is always tender to pressure, although the pain is often temporarily absent, thence it extends to the occiput, neck, shoulder, scapula, arm, forearm, hand, and fingers. There may be sympathetic nervous symptoms of sneezing, rhinorrhea, lacrimation and photophobia, diminished taste over the anterior half of the tongue, bad taste in the mouth, slight moderate sensory disturbance of the soft palate, and at times the attacks may resemble true migraine and at other times nodular headache associated with actual nodules about the occipitofrontalis muscle. There are a host of other peculiar disturbances associated with lesions of this area, and the importance of this syndrome should never be forgotten, nor should one neglect the simple clinical diagnostic point of local cocainization of Meckel's ganglion in obscure symptoms relative to the distribution of the cranial nerves. One may understand the possible complex symptom-

tology in the production of this syndrome when he realizes the nerve trunks which supply the ganglion, namely, the maxillary branch of the fifth and the vidian. It is supplied with sensory fibers by the maxillary. The vidian is composed of the great superficial and deep petrosals. The great superficial petrosal comes from the ganglion bearing motor fibers from the seventh and taste fibers which have arisen in the anterior two-thirds of the tongue that are to reach the brain by the fifth nerve. The great deep petrosal is the sympathetic nerve branch of the carotid plexus and has connection with the superior cervical ganglion and indirectly with the last cervical and first dorsal ganglion which send fibers to the lungs and heart, an anatomic relationship which may explain certain obscure pulmonary and cardiac symptoms associated with nasal pathology. The maxillary and vidian trunks frequently lie in very close association with the sphenoid sinus and may be separated by only an egg-shell thinness of bone. Therefore, when inflammation exists in this cavity it may readily involve the associated nerve trunks, etc., by direct extension or by the toxin passing through the thin bony wall. The differential diagnosis of lesions of the ganglion proper and those of more central origin is made by cocaineization which stops the pain of ganglion lesions, but does not affect the pain of maxillary or vidian nerve lesions.

Dr. Sluder's treatment consists in applying a 2 per cent. solution of silver nitrate over the ganglion, and in obstinate cases he injects  $\frac{1}{2}$  c.c. of 5 per cent. phenol and 95 per cent. alcohol into the ganglion. He has secured remarkable results from the injection of the ganglion in the severe pain and photophobia of glaucoma, iritis, corneal ulcer and the correction of a most pronounced, red and enlarged external nose in addition to striking relief in a variety of other isolated conditions.

The last condition, or hyperplastic sphenoiditis, is a localized inflammation and thickening of the mucosa sometimes associated with polypi and cysts within the sinus. The pain symptoms are naturally due to the association of the nerve trunks in this region including the vidian and the first and second divisions of the fifth. The symptomatology might be similar to that

described under the nasal ganglion neurosis, and the treatment naturally consists in the proper drainage and ventilation of the sinuses.

We forbear from discussing other neuralgias about the head and face, such as the terrifically severe neuralgia of the trifacial or tic douloureux, for which as you know injection of the ganglion is necessary or even resection of the sensory root, which I am sure most of you have fortunately seen in Coughlin's clinic done with remarkable technic under local anesthesia.

The last type of headache which we will consider is the rheumatic. This type usually occurs in people over forty and is ordinarily located in the suboccipital region, radiating to the neck, shoulders, and vertex, often influenced by changes of the weather and exposure to cold winds. Palpation discovers a number of small tender nodules about the aponeurosis of the occipitofrontalis muscle, and the condition may be associated with such general manifestations as fever, leukocytosis, arthritis, and focal manifestations elsewhere. Infected teeth and tonsils may also be at fault. The diagnosis depends upon the presence of the tender indurated areas at the attachment of the muscle to the occiput. Treatment may consist of local application of heat, massage, the clearing up of focal infection, and the administration of such antirheumatic remedies as the salicylates. We had intended to present some interesting clinical types of indurative headache, and of "Sluder's lower half headache," in which, in conjunction with our rhinologist colleagues, we have seen almost dramatic relief from treatment directed to the nasal ganglion, but time forbids and these must await a later presentation.

This concludes our consideration of headache, and I trust that the classification of intracranial and extracranial may simplify the problem in your minds. You can readily appreciate how the great classification of intracranial headache includes a great variety of causes. Recall that Edinger believes that somewhere in the cutaneous and dural branches which supply the affected area lies the cause, and Campbell feels that irritation of the sympathetic nerves running in the vessel walls of the dura and



brain substance produces headache, but whatever the mechanism, any irritation, chemical or physical, producing increased pressure may be responsible for headache. We have briefly outlined the extracranial causes calling your attention directly to the ocular and the various types of nasal etiology. The lesson to be learned is that headache after all is but a symptom, and that an extremely careful search must be made for the causative factor rather than a futile attempt to relieve pain by the remedies you have at your command. I would call your attention particularly to a study of the individual in his entirety and especially to the wide-spread influences of the vegetative nervous system and the endocrines. Without bias, remember pituitary possibilities, the extremely interesting aspects of migraine, and the dramatic phases of nasal ganglion neurosis.

Above all, however, as students realize the broad etiology of headache, the necessity of careful diagnostic investigation into causation instead of expending your energy on a frequently futile attempt at symptomatic relief.



## CLINIC OF DR. ALBERT E. TAUSSIG

FROM THE MEDICAL SERVICE OF THE JEWISH HOSPITAL

### NON-DIABETIC GLYCOSURIA AND NON-GLYCOSURIC DIABETES

THE first cases I have to show you today are two brothers, seventeen and nineteen years old. The older was first brought to see me four years ago, at the age of fifteen. He had had the usual diseases of childhood, but, on the whole, had been considered quite healthy and had been something of an athlete. There had been no occasion for previous urine examinations. It was therefore with great astonishment that he found himself rejected for life insurance as a diabetic. Physical examination showed a healthy looking lad and was in general quite negative except for the presence of a few small hard glands in axillæ, elbows, and groins. The urine, however, with a specific gravity of 1023, contained a trace of albumin, an occasional finely granular cast, about 1 per cent. of sugar, no acetone or diacetic acid. I may say here that the very numerous urine examinations that have been made since then have never again shown the presence of albumin and casts, but have invariably shown the presence of sugar.

A few days after this preliminary examination he entered the Jewish Hospital for study. The reaction of blood and urine sugar to various diets may be summarized in the following table:

Day in hospital.	Diet.	Fasting blood sugar.	Total urine sugar in twenty-four hours.
1	Unrestricted .....	0.080 per cent.	2.5 gm.
2	Starvation.....	0.085 "	2.4 "
3	Starvation.....	"	2.2 "
4	Restricted carbohydrates.....	"	2.4 "
5	Restricted carbohydrates.....	0.070 "	1.9 "
6	Same plus 107 gm. dextrose.....	0.070 "	2.6 "

The striking feature of this table is the total lack of correspondence between the diet and the output of sugar in the urine; with an unrestricted diet, under starvation and when fed an excessive amount of dextrose, the sugar output remained practically unchanged.

The blood sugar curve, after a glucose meal consisting of 94 grams (*i. e.*, 1.75 gm. glucose per kg. of body weight) in lemon juice, showed a similar phenomenon:

Time.	Blood sugar.	Urine sugar.
Fasting . . . . .	0.107 per cent.	0.95 per cent.
One hour after dextrose meal . . . . .	0.110 "	0.90 "
Two hours after dextrose meal . . . . .	0.095 "	0.15 "
Three hours after dextrose meal . . . . .	0.068 "	None.

Here again the lack of response, on the part of both blood sugar and urine sugar to the ingestion of a considerable dose of dextrose, is striking. Another striking feature is the fact that the only time, during this period of observation, that this patient's urine was found free from sugar was on this occasion, three hours after a glucose meal. The tendency of the blood sugar to fall below the normal level and for the urine to become sugar free some hours after the ingestion of a considerable amount of dextrose, is often seen in the type of case under discussion.

During the following three months the patient was put on a moderately restricted diet (*i. e.*, proteins, fats, and 5 per cent. vegetables freely, not over 15 gm. of 5 to 10 per cent. vegetables, and one slice of bread with each meal, no sugar) and continued to feel well, though frequent urine examinations were always positive for sugar. In March, 1920 another blood sugar tolerance test was done, with the following result. The amount of glucose given was again 1.75 gm. per kg. of body weight

Time.	Blood sugar.	Urine sugar.
Fasting . . . . .	0.079 per cent.	0.37 gm.
One hour after dextrose . . . . .	0.093 "	0.17 "
Two hours after dextrose . . . . .	0.104 "	0.12 "
Three hours after dextrose . . . . .	0.093 "	0.01 "

Thereupon the patient was told that his glycosuria was quite innocent and he was put on a completely unrestricted diet as

regards both sugar and starches. He has reported at somewhat frequent intervals; his health has always been perfect, his urine has always contained sugar, ranging from  $\frac{1}{2}$  to 1 per cent., but no other abnormal constituents; blood-sugar tolerance tests, done every six months, have uniformly given results like those tabulated above.

Last July he brought with him this second patient, his brother, a year and a half younger than he. This young man came because, though now seventeen years old, he did not consider himself sufficiently developed sexually. Like his brother, he had never been seriously ill and was something of an athlete. Physical examination was entirely negative, the sexual organs appearing normal. The urine, however, otherwise normal, contained about  $\frac{1}{2}$  per cent. of sugar. This patient refused to submit to the careful study that his brother had undergone, but a blood-sugar tolerance test resulted as follows:

Time.	Blood sugar.	Urine sugar.
Fasting.....	0.125 per cent.	$\frac{1}{2}$ per cent.
One hour after 100 gm. dextrose....	0.111 "	1 "
Two hours after dextrose.....	0.074 "	Trace.
Three hours after dextrose.....	0.108 "	Absent.

Since then he has been on an entirely unrestricted diet, has been entirely well in every way, while his urine has uniformly contained about  $\frac{1}{2}$  per cent. of sugar.

The main characteristics of the disorder illustrated by our 2 cases may be summarized as follows:

1. A constantly normal or subnormal blood sugar, influenced slightly or not at all by the ingestion of large amounts of dextrose.
2. A constant, or nearly constant glycosuria, independent, or nearly so, of the carbohydrate intake; this is due to an extremely low blood-sugar threshold for the production of a glycosuria.
3. The absence of all symptoms suggestive of diabetes mellitus and the uniformly benign character of the disturbance.
4. The youth of the patient; where this disorder is first

discovered in adult life, it may well be that it had existed undetected for many years.

5. Its tendency to run in families. Solomon was the first to call attention to this in 1914; Brugsch and Drexel in 1919 showed that, so far as can be made out from a somewhat limited material, it seems to follow the mendelian law.

Of these characteristics, the first three appear to be the essential ones and should be present if a case is to be classed with this group. Whether patients that show the first two characteristics can ever be on the way to a true diabetes, as Joslin suspects, may, in the present state of our knowledge, seem improbable; but this possibility cannot be absolutely denied until they have been observed over a considerable period of time.

The name to be given to this disorder presents some difficulty. On account of its apparent resemblance to the glycosuria following phloridzin injections, it has generally been called "renal diabetes" or "renal glycosuria." This name seems undesirable for two reasons: First, it takes for granted that the disorder is due to a renal abnormality, a matter that is far from certain. Second, this name would appear more suitable to the large group of cases, studied chiefly by the Germans, in which a relatively high blood sugar with glycosuria gradually develops in the course of a chronic nephritis.

Solomon has suggested the name "innocent diabetes." This is doubtless better and is objectionable only because it suggests a relationship between our patients' disorder and true diabetes mellitus. An adequate name will probably not be found until the etiology of the disorder is cleared up. In diabetes it has been shown that the blood sugar differs in kind from that present in health; it is this abnormal blood-sugar that is excreted by the kidneys. If a similar abnormality in the blood sugar were to be found in the so-called "renal glycosuria," but here without pancreatic insufficiency, this would best explain the observed phenomena.

The third patient to be presented illustrates a group of cases closely allied to the one just considered, but differing in

one important respect. He, too, shows a blood sugar influenced but slightly by the ingestion of large amounts of glucose. He, also, is entirely symptom free. His blood-sugar threshold for the production of glycosuria is also abnormally low, but, as will be seen, the glycosuria in his case is not entirely independent of the amount of carbohydrate ingested.

The patient is forty-nine years old, a manufacturer, married, with two healthy children. His family and previous history are practically negative; he has always been fond of sweets and has never shown any symptoms suggestive of diabetes. In 1922 he passed for life insurance.

In November, 1922, while playing cards in the evening, he suddenly fainted. The loss of consciousness lasted less than a minute, there was no convulsion, and by the time I got to him he was quite himself again. He had never fainted before and has had no similar attack since. Routine physical examination was negative, but the urine, examined the next day, contained about 2 per cent. of sugar. Some weeks later he entered the Jewish Hospital of St. Louis for a careful going over, and has returned from time to time for a metabolic study.

The patient is a somewhat spare man, but looks entirely well. Physical examination gives findings quite normal in every respect. The blood, too, shows no abnormality, Wassermann negative, N. P. N. 32 mg. The urine occasionally contains a trace of albumin and an occasional granular cast; P. S. P. 46 per cent. in the first hour, 24 per cent. in the second.

In January, 1923 the blood-sugar tolerance was as follows, the meal consisting of 1.75 gm. dextrose per kg. of body weight:

Time.	Blood sugar.	Urine sugar.
Fasting.....	0.110 per cent.	Absent.
One hour after dextrose meal.....	0.135 "	Present.
Two hours after dextrose meal.....	0.110 "	"
Three hours after dextrose meal....	0.065 "	"

Ten days later another blood-sugar test was made, the meal this time consisting of protein 50 gm., carbohydrate 50 gm., fat ad. lib.:

Time.	Blood sugar.	Urine sugar.
Fasting.....	0.118 per cent.	None.
One hour after meal.....	0.129 "	1.1 gm.
Two hours after meal.....	0.121 "	1.0 "
Four hours after meal.....	0.125 "	2.3 "
Six hours after meal.....	0.119 "	None.

More recently a blood-sugar tolerance test, with 100 gm. dextrose, gave the following result:

Time.	Blood sugar	Urine sugar.
Fasting.....	0.100 per cent.	Absent.
One hour after dextrose.....	0.190 "	Present.
Two hours after dextrose.....	0.117 "	"
Three hours after dextrose.....	0.088 "	"

A study of the protein and carbohydrate tolerance, extending over a considerable period of time, shows that he can manage practically indefinite amounts of protein if the carbohydrate is kept low, but that, if the daily carbohydrate intake reaches 60 gm., or if he takes more than 18 gm. of carbohydrate at a single meal, sugar invariably appears in the urine. If less than this amount of carbohydrate is consumed, the urine constantly remains sugar free.

The case thus appears to lie on the borderline between the so-called renal diabetes and true diabetes mellitus. On the one hand, the blood-sugar is normal, is but slightly influenced by the ingestion of large amounts of carbohydrate, and shows an abnormally low threshold for the production of glycosuria; on the other hand, the appearance of sugar in the urine is very directly dependent upon the amount of carbohydrate eaten. Whether these cases should be considered as entirely innocent, or whether they may later slip over into the true diabetes mellitus, only time can tell. Studies such as these are as yet too recent to furnish a definite reply to this question. In the case of our patient we have preferred to play safe and to treat him as though he were a diabetic. A bearable diet has been worked out, on which he maintains his weight and puts out only traces of sugar in the urine.

Finally, I wish to present 2 cases that, in their blood and urine findings, are the exact opposites of the preceding ones:

W. E., aged forty-five years, a merchant, consulted me for an annoying pruritus ani. He comes of an eminently diabetic family, but his own previous history is entirely negative. Except for the pruritus, he feels perfectly well. Physical examination shows normal findings; the urine has a specific gravity of 1009 and is free from abnormal constituents, even on an unrestricted diet containing much sugar; the blood-count and blood-picture are normal, Wassermann negative, the stool is free from ova or parasites. Our proctologist pronounces the pruritus as due to a low-grade rectal infection, and states that cases of this sort are not infrequently seen by the men of his specialty. Nevertheless, in view of his family history, a blood-sugar tolerance test was done, with the following result:

Time.	Blood sugar.	Urine sugar.
Fasting . . . . .	0.157 per cent.	Absent.
One-half hour after taking 100 gm. dextrose . . . . .	0.222 "	"
One hour after dextrose . . . . .	0.200 "	"
Two hours after dextrose . . . . .	0.200 "	"
Three hours after dextrose . . . . .	0.125 "	"

A. S., aged forty-eight, a broker, was referred from the surgical service on account of a furunculosis, culminating in a carbuncle of the neck. He does not come of a diabetic family and his previous history is entirely negative; indeed, except for this attack of furunculosis he has had no untoward symptoms since childhood. Physical examination gives entirely normal findings; the blood-count and blood-picture are normal, Wassermann negative; urine entirely normal, even on an unrestricted diet containing much sugar. The blood-sugar tolerance, done on account of the furunculosis, was as follows:

Time.	Blood sugar.	Urine sugar.
Fasting . . . . .	0.200 per cent.	Absent.
One-half hour after 100 gm. dextrose . . . . .	0.240 "	Trace.
One hour after dextrose . . . . .	0.250 "	0.5 per cent.
Two hours after dextrose . . . . .	0.204 "	0.5 "
Three hours after dextrose . . . . .	0.166 "	Absent.

These cases, it is clear, show the typical blood-sugar curve of diabetes mellitus, as well as the high threshold for glycosuria, characteristic of this disease. On the other hand, except for these blood findings, there is nothing in either case that would justify the diagnosis of diabetes mellitus. Such a situation is not infrequently met with in old cases of diabetes, in whom a high-grade interstitial nephritis has led to the disappearance of the sugar from the urine. Our cases are obviously not of this sort: they are neither old diabetics nor have they a nephritis. We must consider them as truly prediabetic, in the sense that they appear to show a strong tendency toward this disease and that, left to themselves, they might be expected in the course of time to develop a frank diabetes. The situation has been explained to them and they have been put on a moderately restricted diet, one from which sugar has been excluded and the intake of starch limited. What the ultimate outcome will be only time can tell.



## CLINIC OF DR. GEORGE W. WILSON<sup>1</sup>

BARNES HOSPITAL

### INFLUENZA

**Discussion of Etiology: The Rôle Played by the Bacillus of Pfeiffer, Bacterium Pneumosintes. Secondary Invaders. Pathology. Symptomatology. Type Cases. Complications. Sequelæ. Treatment. Vaccination.**

It is interesting to note that the name "influenza" comes from a Spanish word meaning influence, which many years ago was mistranslated by a medical writer who described the disease which today we know as influenza. In the diagnosis of this condition one is forced to the conclusion that as much confusion exists in this regard today as must have existed in the mind of the aforesaid translator. We find the common cold, various infections of the nasopharynx, tonsils, larynx, trachea, and lungs all diagnosed influenza.

It is just five years ago since the first wave of the influenzal pandemic of 1918-19-20 made its appearance. The confusion as to just what this disease is has to a degree been dispelled. In fact, thanks to untiring clinical observation and experimental methods of research, our present knowledge should enable one to make a very accurate diagnosis. True, in isolated and sporadic cases the diagnosis may be somewhat difficult: however, if definite requisites are laid down and met with, the clinician can usually set aside all reasonable doubts concerning the condition present. At the outset, a definition of influenza might be valuable. It might be defined as an acute infectious disease:

<sup>1</sup>From the Department of Internal Medicine, Washington University Medical School.

characterized by catarrhal inflammation of the upper respiratory tract with angina, general muscular aching, fever, with relatively slow pulse of four to five days' duration, prostration out of proportion to physical findings and leukopenia—very rarely fatal itself, but predisposing to secondary fatal lung affections.

**Etiology.**—*The Predisposing Factors.*—*Age:* Young adults between the ages of twenty to forty years are most frequently attacked. Old people are relatively immune, also very young children. *Sex:* Males are attacked more frequently than females, this probably on account of the greater opportunity for exposure. *Race:* Probably not important. *Climate:* This probably plays a very small rôle, as is shown by the pandemic character of the epidemics of 1890 and 1918. *Seasons,* too, are not a determining factor. *Exposure* to cold, mental and physical fatigue, as for all infections, lower bodily resistance.

*Exciting Causes.*—Following the epidemic of 1890 Pfeiffer announced that a very minute Gram-negative bacillus isolated from the throats of individuals suffering with influenza was undoubtedly the cause of influenza. This organism was also found in the lungs of persons dying with complicating pneumonia and in the throats of certain healthy individuals, at this time thought to be carriers. Those convalescing from attacks of influenza also frequently showed its presence. The names "bacillus of Pfeiffer and *Bacillus influenzae*" were given, and it was generally conceded that this organism was the cause of epidemic influenza. Later many observed that the *Bacillus influenzae* occurred in the throats of healthy individuals with no reference whatsoever to epidemics of influenza, and of children suffering with measles and other affections. At times it was absent in very frank cases of influenza: however, with the advent of the epidemic of 1918, various methods were immediately employed for the most efficient isolation and cultivation of the "*Bacillus of influenza*," the admitted cause. At once many conflicting reports emanated from various bacteriologists. It was not possible in all instances of influenza to demonstrate the presence of the Pfeiffer bacillus. On the other hand, many cases showing disease other than influenza showed its presence

and perfectly healthy individuals harbored it. Some workers report its occurrence in uncomplicated influenza pneumonia in as high as 92 per cent. of the cases, and have gone on record as definitely describing it as the etiologic agent in this disease.

Livierato, while unwilling to admit that the problem is definitely solved, is personally inclined to consider that Pfeiffer's bacillus is the specific pathogenic agent in influenza. Experiments of McIntosh, who was able to demonstrate in considerable numbers *Bacillus influenzae* in the upper respiratory tract (75 to 80 per cent. of his cases and later in the lungs in large numbers) are oft quoted by those who hold to influenza as the etiologic agent. McIntosh also carried out serologic examinations in the form of complement-fixation and agglutination tests on the serum of convalescent patients. He reports that in the vast majority of these tests antibodies for the *Bacillus influenzae* were present. For and against the bacillus Zinsser sums up somewhat as follows in favor of attributing entire processes to influenza bacilli: (1) The frequent isolation of bacilli even in earliest and simple cases. (2) The high percentage of influenza bacillus isolation from all varieties of early and late complications. (3) The peculiar distribution of these bacilli in the large and small bronchi in fatal cases. (4) The frequent presence in culture at necropsy. (5) Their extensive distribution throughout populations during an epidemic. (6) Their gradual diminution in frequency in normal throats and respiratory spaces as epidemics decline. Against this etiologic importance of the influenza bacilli are exposed: (1) The frequent failure of competent bacteriologists to find the organism in early cases. (2) The presence of the bacilli in the throats of normal individuals. (3) Their presence in conditions obviously non-influenzal clinically. (4) Their frequent presence as secondary invaders in whooping-cough, measles, etc. (5) The antigenic multiplicity of strains isolated during an epidemic. (6) The infrequency of positive blood-cultures in early cases. Tests for antibodies have been unconvincing, as have protection experiments with vaccines. Zinsser concludes that the burden of evidence points to the probable causation by the influenza bacillus, but there are certain elements of

uncertainty. The greatest element to my mind, and almost if not convincing proof to the contrary, is the work of Olitsky and Gates, who have been able to isolate from early cases of influenza a filterable infectious agent named by them "*Bacterium pneumosintes*," with which they have been able to produce in rabbits a condition very closely simulating influenza. They call attention to the necessity of recognizing influenza as a specific primary disease and to relegating various bacterial pneumonias that develop in influenza-injured lungs to the rôle of secondary infection. Without this proviso one could readily ascribe to the various secondary invaders met with in influenza the same rôle that has been ascribed to the influenza bacillus, viz., the etiologic agent. The more important of these are the *Micrococcus catarrhalis*, streptococci, pneumococci, bacillus of Friedländer, and *Staphylococcus aureus*. In addition, they have called attention to the importance of epidemic influenza in its early stages before secondary infection has obscured its specific character. All investigations were based on uncomplicated cases within thirty-six hours after the onset, which is described as usually sudden with a chill or chilly sensations and fever, headache, and general muscular pains, especially in the back. In the severe cases the prostration that accompanies these symptoms forces the patient to bed, the eyes become inflamed and sensitive to light, the face is suffused, the throat edematous and raw, a thin irritating secretion flows from the nose, and the progress of the infection is accompanied by hoarseness and a dry and distressing bronchial cough. Examination of the chest reveals no certain signs of lung involvement and other organs are not usually obviously affected, pulse and respiration are only slightly accelerated, the temperature remains fairly constant between 101° to 103° F. for three or four days, and then, after profuse perspiration, falls rapidly to normal with the onset of convalescence.

Olitsky and Gates call attention to the leukopenia, affecting particularly the mononuclear cells. In 1918 nasal washings from such cases within the first thirty-six hours after onset were used for monkey inoculation. The results were more or

less indifferent. Later the rabbit was chosen as the experimental animal, and what seemed to be typical influenza resulted. The rabbits appeared ill with ruffled fur, conjunctivitis, fever, and showed definite depression of the leukocyte count. If they were killed at the height of the attack and there had been no secondary infection the lungs were found to be distended with edema in the inner alveolar walls and by large emphysematous spaces due to their rupture. On section, they were mottled with large and small hemorrhages in the substance of the lung. There was a very scanty cellular exudate of mononuclear and polynuclear cells, the bronchi contained fluid and exfoliation of the epithelium. There were never definite signs of consolidation and in most instances none of the ordinary bacteria could be recovered. This picture was produced both by filtered (Bergfeld) and unfiltered nasopharyngeal washings, and the picture was reproduced through many series of animals.

A very interesting observation which coincides with the idea expressed by many early observers to the effect that the cause of influenza, whatever it might be, predisposed to invasion by bacteria ordinarily known to be non-pathogenic or causing very little disturbance was made. Namely, when unfiltered nasopharyngeal washes were used for intratracheal inoculations various lesions were produced by the secondary invaders. It was found that ordinary pulmonary resistance to the pneumococcus, streptococcus, and bacillus of Pfeiffer was decreased, this also was true when the virus was injected intravenously and the animals inoculated intratracheally with the secondary invaders. The "Bacterium pneumosintes" of Olitsky and Gates can be cultivated on the Smith-Nagouchi culture-medium which consists of sterile ascitic fluid or dilute serum to which is added a small fragment of fresh sterile kidney, usually from the rabbit. Growth occurs under strictly anaërobic conditions. In appearance they resemble the globoid bodies of poliomyelitis in size, but tend toward bacilli in form. They are Gram negative. In 1922 and again in 1923 the same bacterium was isolated from "pure" cases of influenza. Animals immunized with a vaccine of *Bacterium pneumosintes* are rendered immune to experimental

production of lesions with pathogenic washings and cultures. Agglutinins have been demonstrated in both the blood of humans and animals so immunized. The blood of recovered influenza patients contains agglutinins for *Bacterium pneumosintes*. The foregoing is an outline of the work of Olitzky and Gates. In many instances their own words have been used as offering a more accurate account.

It would seem that their investigations offer very strong if not conclusive evidence in favor of the etiologic significance of *Bacterium pneumosintes*.

**Pathology.**—On account of the almost universal association of early complications with influenza and the recovery of mild uncomplicated cases it has been rather difficult to arrive at an exact concept of the anatomic changes in cases of pure influenza. McCallum, however, toward the end of the epidemic of 1918, called attention to the anatomic lesions of the pneumonias following influenza. Aside from the ordinary features peculiar to pneumonias caused by the various secondary invaders, most important of which are the *Streptococcus hemolyticus*, *pneumococcus*, *bacillus of Friedländer*, *Micrococcus catarrhalis*, and *Staphylococcus aureus*; the lungs examined by him presented certain definite characteristics. He stresses especially the hemorrhagic character of the tissue in which the ductuli alveolares are lined with a hyaline membrane and are filled with fluid. This hyaline-like substance forms a thin layer on the bronchioles down into the alveoli. It is of a character not seen in pneumonias following any condition other than influenza, and possibly poison gases. McCallum also describes the several modifications of the anatomic picture which are determined by the type of secondary invader. There is a very constant and definite picture in pneumonias caused solely by the influenza bacillus. I have been unable to find a satisfactory description of postmortem examinations of lungs in what might strictly be termed "uncomplicated influenza." The question of secondary invaders must always come up. However, certain cases are described in which death occurred within from thirty-six to forty-eight hours after onset. These closely correspond

in pathology to that produced in experimental influenza, a description of which follows. Baehr and Loewe, summing up their findings in the lungs of rabbits inoculated by intratracheal insufflation of the filtrates (Berkefeld) of nasopharyngeal washings from early cases of influenza and the cultures from such washings, summarize as follows: (1) Congestion, edema, and small hemorrhages in the mucous membrane of the trachea and bronchi. (2) The presence of a profuse slightly blood-tinged serous liquid in the lumina of the bronchi. (3) Diffuse distribution of red jelly-like substance throughout the lungs. (4) Injected condition of a large part of the intervening lung and acute emphysema, with distention of the alveoli. (5) Exudation of serous and red blood-cells from the vessels filling interstitial tissues and groups of alveolar air-passages. (7) Dilatation of short stretches of capillaries and arteries and sometimes closure of the lumina of these vessels by blood-clot. (8) Tendency to early secondary invasion with pyogenic organisms, which then induce a rapid purulent infiltration, thereby completely obliterating the primary and specific picture of the disease. It will be seen that these findings correspond very closely to the cases of complicated influenza in humans coming to autopsy; also to the picture of experimental influenza produced by the *Bacterium pneumosintes* of Gates and Olitzky. From the above and also from clinical grounds it seems reasonable to conclude that influenza is a definite disease with characteristics peculiar unto itself, although not always in evidence on account of early secondary infection. A description of the pathology of the various complicating conditions is beyond the scope of our present discussion, which involves uncomplicated influenza only.

**Immunity.**—There seems to be a definite immunity conferred by an attack of influenza. This is borne out both clinically and experimentally. Clinically, by the observation during the epidemic of 1918, that comparatively few or none of the individuals who gave histories of an attack in 1890 were attacked in the last named epidemic. Casieres collected data from the epidemic of 1921 and 1922, and found that 92 per cent. of the patients who had contracted the disease during the 1918 epidemic



had been spared during the present one, and that the remaining 8 per cent. had been affected only very slightly; this in spite of the deplorable hygienic conditions of life in the small towns and other untoward predisposing factors. Casieres experiments seem to show that influenza confers actual immunity which lasts at least three years. Experimentally, Olitzky and Gates have demonstrated the presence of immunity in animals subsequent to survival of an attack of experimental influenza. Also the production of immunity by vaccine.

**Diagnosis.**—The diagnosis of influenza during an epidemic is comparatively easy; the danger at this time is rather that of taking all respiratory affections for influenza rather than missing a case. The sporadic cases offer difficulty. At the outset it is well to remember that influenza is a very definite clinical entity. Certain constant symptoms should be present for a positive diagnosis. Ordinarily a non-complicated case starts with general feelings of malaise, chill or chilly sensations, abrupt rise of temperature, general aching of practically all muscles of the body, especially the back and shoulders, slight joint pains, sore throat, which is described by the patient as scratchy, and more or less prostration. The temperature varies from 100° to 103° F. Very important, the pulse-rate may be increased very slightly if at all, but more often is normal or even decreased below the normal, this without reference to height of the fever. Early there is a dry cough which is quite troublesome, and when severe greatly tends to fatigue the patient. Later this cough may be accompanied by a thin serous mucous exudate. In very severe cases the sputum may become blood-streaked and actually hemorrhagic in character.

**Physical examination** shows slight injection of the conjunctivæ and possibly some lacrimation, a thin scanty mucous discharge from the nose, definite congestion of the mucous membranes of the mouth and pharynx, with very little if any exudate.

Bloomfield and Harrops' description of oral and pharyngeal findings is excellent and should be quoted at this point: "The most striking feature is a bright vermilion or scarlet injection



of the pharynx, tonsils, pillars, and soft palate. In many cases this erythema extends over the entire mouth, and can be exquisitely demonstrated by pressure on the mucosa of the cheek with a spatula. In the most marked cases the entire mouth cavity has a flaming appearance. On analysis, this redness is seen to be due to a diffuse hyperemia of the mucous membrane, together with an injection of minute blood-vessels on the pharynx and pillars, but especially on the soft palate. There is a line of demarcation at the hard palate, which is relatively free. In some cases, especially the mild ones, these changes are less marked, being confined to the soft palate and pillars. There is extreme swelling of the lymphoid tissue of the posterior pharyngeal wall, which gives it a remarkable corrugated appearance. These changes are clearly in the nature of an erythema, and there is never any localized exudate.

"The tongue is usually coated, but if clean is bright red like the buccal mucosa.

"In from one-half to two-thirds of the cases at onset one to three or four, or even more, dark crimson spots were seen on the mucosa of the inside of the cheek. They were occasionally present on the gums, soft palate, mucous border of the lips, or on the uvula. These spots vary from a minute pin-point up to 1 millimeter in diameter and may be arranged in one or more clusters. The dark cherry color and sharp margin characterize them and seem to indicate that they are of hemorrhagic origin. The individual spots fade rapidly, disappearing without trace in from one to two days. They may reappear in repeated crops in the same individual, and are seen in convalescence in most of the cases. About 94 per cent. of our patients in whom they were systematically looked for showed them at some time during the course of the disease." They conclude that their cause is uncertain, but that their presence may have a degree of clinical specificity.

The lungs in early cases show absolutely no physical change, later there may be harshened breath sounds and occasional rhonchi. On the whole, the patient presents the appearance of one who is quite sick, but out of proportion to demonstrable

physical findings. Occasionally cases complain of gastro-intestinal symptoms which take the form of nausea, general abdominal pain, and at times diarrhea.

**Laboratory Findings.**—The urine is generally negative, bacteriologic examination of the sputum may reveal the presence of any of the secondary invader organisms discussed under pathology. The blood shows either a normal number of leukocytes or a definite decrease, at times as low as 2000 per cubic millimeter, a very *important* finding. According to Olitsky and Gates this decrease affects the mononuclear cells, some report a relative increase of the lymphocytes. Later, depending on complications, the blood-picture may change. Thus, on invasion of the pneumococcus, staphylococcus, etc., the blood-count may go up, the leukocytosis affecting the polymorphonuclear leukocytes. This does not hold true where bacillus of influenza is the secondary invader. The sputum is changed in complicating pneumonia. Liebman lays particular stress on its sudden change from the hemorrhagic to purulent type, also, its increase in amount and reduced tenacity. Microscopically we find the appearance of elastic fibers, predominance of polymorphonuclear leukocytes showing degenerative changes, and the appearance of abundant macrophages loaded with cellular debris. Liebman thinks these last cells are scavengers of the alveolar walls.

We shall now view a case demonstrating the foregoing.

**Case I.**—Male. Age twenty-six. Admission note: Patient enters hospital with history of chills and fever, three chills during the last few days, no sweating, vomiting or nausea or diarrhea. Has been coughing past few days with reddish-brown expectoration, no chest pains, has had some cramps in lower abdomen. Eyes are red, patient very drowsy and dull, does not answer questions promptly, throat injected, tonsils somewhat enlarged. Examination of chest negative, temperature 103° F., pulse-rate 80. Heart negative, abdomen soft, there is no muscle spasm or tenderness to deep pressure. Slight watery discharge from nose. White blood-count is 4900, smear shows predomi-

nance of mononuclear cells. Tentative diagnosis is typhoid or influenza.

*Detailed History.*—*Chief complaints:* General weakness, chills and fever, loss of appetite, family history unimportant. *Past history:* Measles, whooping-cough, pneumonia six years ago, no history of influenza, occasional sore throat, otherwise negative.

*Present Illness.*—Onset four days ago. Slight sore throat accompanied by headache.

Patient says he felt as though he had some fever. Slight chill three days ago, no sweats. There has been a nasal discharge during past two days, also cough, no expectoration other than small amount of phlegm. Mild pains in back and legs, slight epistaxis yesterday. White blood-count 4600, red blood-count 5,700,000. Hemoglobin 84 per cent., polymorphonuclears 41 per cent., no basophils, large mononuclears 3.4 per cent., lymphocytes 56 per cent., nothing abnormal in smear. Phthalein 6 per cent. first hour, 10 per cent. second hour. Temperature at entrance 103° F., pulse-rate 75, with gradual declination to the third day, when pulse-rate was 68 and temperature normal. *Physical examination:* Patient appears quite sick, there is slight coryza, face flushed and suffused, some lacrimation and photophobia, patient coughs a great deal. Tonsils slightly enlarged and injected, also the pharynx. Chest is resonant throughout and generally negative. Heart also negative, abdomen negative. Tentative diagnoses: Influenza(?), coryza, chronic tonsillitis, typhoid(?), malaria(?).

Blood-culture negative, Widal done two days later negative. At this time white blood-cells 3700, gradual decline of temperature. Sputum shows a Gram-negative bacillus, blood-pressure 90 systolic, 50 diastolic, with a gradual rise until discharged five days later, systolic 100 and diastolic 60. Urine shows slight trace of albumin, sediment negative. Comment: An uncomplicated case of pure influenza. Treatment: Rest in bed, soft diet. Recovery uneventful.

**Case II.**—Female, age thirty-two. Patient enters hospital complaining of nasal discharge, cough which is unproductive,

fever, and feeling generally bad. White blood-count on entrance 4100, red blood-count 4,800,000, hemoglobin 80 per cent., Wassermann negative. Phthalein test 60 first hour, 23 second hour.

*Physical Examination.*—Slight tenderness over both mastoids, nose negative, pharynx congested, no exudate.

Chest shows hyperresonance throughout, breath sounds increased, and there is a slight prolongation of expiration at the left apex anteriorly. Posterior the breath sounds are increased at the right apex. There are a few moist râles in the right interscapular area at the end of inspiration. Voice sounds negative, heart sounds negative. Blood-pressure systolic 110, diastolic 66, pulse-rate 94.

Abdomen: There is slight tenderness just to the right of the midline above the umbilicus, also general tenderness throughout the lower abdomen. Right kidney is palpable. Family history unimportant. Past history: Chickenpox, measles, pertussis, frequent sore throats, appendectomy 1914, history of cholecystitis.

Present Illness: Pains all over body one week ago, slight discharge from the nose, scratchy feeling in the throat, slight fever, no history of chills. Additional physical examination two days after entrance. Increased tactile fremitus over right apex which is slightly more resonant than the left. Right base posterior less resonant than the left, also few dry râles in the second intercostal space anterior. Inspiration prolonged over right upper posterior. Today, two days after entrance, the white blood-count is 5700, examination of sputum negative for elastic tissue and acid-fast bacilli. Differential count at this time: polymorphonuclears 45 per cent., lymphocytes 40 per cent., large mononuclears and transitionals 14 per cent., otherwise negative. Subsequent examination of the chest shows no râles. Examination of the urine negative. Roentgenogram of the chest generally negative. The pulse-temperature chart at entrance: Temperature 101° F., with gradual decline reaching the normal on the fifth day. Pulse-rate 100, reaching 70 on the fifth day.

*Therapy.*—Rest in bed, sodium salicylate, gr. x every four

hours; codein, gm. 0.015 p. r. n., for cough and pain. Uneventful recovery. Comment: Uncomplicated influenza.

Under diagnosis attention must be called to a fulminant form, of which probably is uncomplicated influenza. In this form the onset is more severe than in the average attack, the patient shows early suffusion and cyanosis of the face, shoulders, and nail beds. The respiration becomes very rapid and within a very few hours there are signs of pulmonary edema; cough with bloody expectoration is the rule, and death comes within twenty-four to forty-eight hours, the patient literally drowning in his own fluid. In this type, as in the uncomplicated type, the leukocyte count is lower than normal, the pulse-rate remains low until the approach of death, respiration is very rapid, as high as 60, and the temperature seems to continue rising until death. In one case the history of which is appended the temperature reached 108° F.

**Case III.**—Male, age thirty. Patient enters hospital with history of becoming sick six days prior to entrance; no other information obtained. (Additional information from friends.) Family history negative. Past history not important.

Present Illness: Patient felt badly four days ago, no nausea or vomiting at this time. Three days ago went to usual business, later returned feeling very sick, had to go to bed. Chief complaints are pain in the back, headache, some nausea and vomiting, generalized pains, especially in legs. Osteopath was called, with no improvement. Later patient became delirious and had to be restrained.

*Physical Examination.*—On entrance patient somewhat irrational, is not orientated as to place and does not appreciate his condition, says he was cured of influenza several days ago by osteopath. Temperature 103.6° F., pulse 100, leukocyte count 4000. Physical examination shows dyspnea, both the lips and nails are particularly cyanotic, general suffusion and injection of the face, pharynx slightly injected.

Examination of the chest: Rapid respiration, breath sounds

at both bases tubular in quality. There is impaired percussion note, also increased whispered voice sounds and tactile fremitus, in both interscapular regions a few dry râles are heard. The abdomen is negative, as is also the rest of the body.

The following day patient showed marked pallor, deep cyanosis with scattered râles over both sides of the chest. Weakness is present, but there are no definite signs of consolidation at this time. Blood-pressure has dropped to 62 systolic. The administration of 15 drops of 1 : 1000 adrenalin solution caused it to immediately rise to 85. Thirty minutes after the injection of adrenalin the systolic pressure became 120 and the diastolic 90, respirations at this time were 54, pulse 140, heart generally negative with the exception of general weakness of sounds; on the next day signs of pulmonary edema rapidly developed and patient died the following morning.

The urine showed a definite trace of albumin and few granular casts; the day before death the pulse-rate rapidly rose to 160, with a decline of temperature from 104° to 101° F.; on the day of death the temperature rising again to 106° F. Final diagnosis on this case was influenza complicated by pneumonia, edema of the lungs and acute bronchitis; no postmortem was obtained. Comment: Probably a case of so-called fulminant influenza.

**Case IV.**—Female, married, age thirty-three. Enters hospital with complaint of becoming sick one week ago, had chill, fever, epistaxis, pain about the eyes, cough with scanty expectoration; later severe pains in chest on coughing, complains of shortness of breath since onset of illness, gives history of being exposed to influenza. Admission note states that patient looks very sick and there is marked dyspnea with cyanosis of nail beds, lips, and ears. Throat is congested. There is a small amount of grayish exudate covering the pharynx. Rapid examination of chest shows exaggerated breath sounds both inspiratory and expiratory over entire chest, increased tactile fremitus, no râles. Heart negative. There is distinct impairment of percussion note at the angle of the scapula on the right

side and dulness below this. There is also impaired resonance over the left base. Here the breath sounds are blowing in character and expiration is prolonged. Numerous crackling râles are heard over the entire chest, especially over both bases. Bronchophony can be made out over the right base. Tentative diagnosis: Influenza and bronchopneumonia.

Later examination shows impairment of percussion note right axilla, also tubular breathing in left axilla; there are a few râles in the left axilla low down. Breath sounds diminished in the right axilla, also bronchophony in the left axilla posterior. Percussion note resonant on the left side; however, there are many crackling râles at left base up to the middle of the scapula. On the right side there is dulness below the scapula, also crackling râles. Whispered voice is increased at the right base and there is also definite suggestion of tubular breathing here. The diagnosis at this time is influenza with bronchopneumonia of right base and left middle lobe. The blood-count on entrance: White blood-cells 6200, on the following day 6400, and the third day 6500. The urine showed large amount of albumin and sediment is loaded with hyaline and coarsely granular casts. Blood-culture is negative, Wassermann negative, the sputum shows pneumococcus and is mucopurulent in character, otherwise negative. Blood-pressure at time of entrance until death ranged from 140 to 120 systolic and from 80 to 65 diastolic. Temperature on entrance 104° F. and pulse-rate 80. Shortly after entrance the temperature dropped to 101° F., pulse-rate remained about the same, and on the following day there was a gradual rise of temperature, until the fifth day it reached 104½° F., and the pulse-rate gradually came up, reaching 100, and on the fifth day 120, at which time the patient died. A few hours before death there was noted rapidly progressing edema of both lungs. Clinical diagnosis: Influenza followed by bronchopneumonia, both right and left sides, edema of the lungs.

Postmortem: Anatomic diagnosis, clinically: Influenza, acute bronchitis, bronchopneumonia, edema of the lungs, including swelling of the viscera. Bacteriologic examination smears from the lung and culture show pneumococcus. Heart negative



except for hemorrhage seen in pericardium. The lungs: Both lower lobes in the posterior portion are extremely congested, are dark purple in color and pit on pressure, there are many firmly consolidated areas which are slightly elevated above the surrounding edematous tissue. Microscopic section of the lungs show alveoli filled with exudate. In some groups of alveoli the exudate is composed mainly of polymorpholeukocytes, in other groups, of red blood-cells with large mononuclear cells and a few polynuclear leukocytes. In many small and larger bronchi the mucous membrane has entirely disappeared, leaving only the bundles of muscle tissue as indicative of the bronchi. Here the purulent content of the bronchus is composed for its greater part of broken-down cells adjacent to the alveoli.

Gastro-intestinal forms of influenza have been described. There are cases in which the respiratory symptoms play a non-prominent rôle, all other than the general symptoms of fever and prostration being confined to the gastro-intestinal tract. These take the form of nasuea, vomiting, and diarrhea, making the differentiation from cases of dysentery difficult. There is also abdominal pain occasionally localized in the gall-bladder or appendix region or epigastrium, causing one to think of an "acute abdomen."

Nervous forms have been described. These have high temperature, great prostration, and nervous manifestations in the form of intense restlessness, delirium, and even mania, or, on the other hand, depression, general apathy, and coma.

Many cases of meningitis have been reported in which the *Bacillus influenzae* has been recovered from the spinal fluid. This should be regarded as a secondary invader. In the present state of our knowledge we cannot say whether the true cause of uncomplicated influenza gives rise to meningitis.

**Differential Diagnosis.**—Influenza must be differentiated from ordinary coryza, pharyngitis, tracheitis, and bronchitis, the causes of which are usually the streptococcus, *Micrococcus catarrhalis*, pneumococcus, usually Type 4, and probably a hitherto unisolated virus. The differentiation is usually simple in these cases, as the prostration, severe muscular pains and



backache found in influenza are usually absent. During an epidemic, in case of doubt it is better to treat all such cases as influenza. Acute pharyngitis or tonsillitis should offer no difficulty, as in influenza the tonsils are rarely if ever enlarged and at most only slightly congested.

At times an uncomplicated lobar pneumonia may offer some difficulty, especially when the process is central and there are no physical findings indicating lobar consolidation. We may also have a silent pneumonia of any type when the focus of consolidation is surrounded by a thick layer of healthy tissue giving rise to no stethoscopic signs. The percussion note also may remain unchanged. Occasionally in a case of central pneumonia one may meet with a zone of exaggerated resonance at the level of the lobe affected by the central process. There is a decrease of vocal fremitus and a diminution of the vesicular murmur at this area, the explanation given being that there is a compensatory emphysema about the consolidation. Absence of pharyngitis, the presence of leukocytosis of the polymorphonuclear variety, and increased respiratory rate are suggestive of "silent" lobar pneumonia rather than uncomplicated influenza, also the isolation of pneumococci from the sputum. This is especially true of Types 1, 2, and 3 of the pneumococcus, Type 4 often being parasitic in normal throats.

*Bronchopneumonia.*—The onset of bronchopneumonia is ordinarily not sudden, most bronchopneumonias being secondary to bronchitis or other infectious diseases involving the respiratory passages. Here the history will in most cases furnish the clue. Pure influenza may be confused with *dengue*. In the presence of epidemics of either disease the diagnosis will not be difficult. However, where there are sporadic cases of each, difficulty will arise during the first two or three days of the disease. The manner of onset and initial symptoms of *dengue* are almost identical with those of influenza; however, the pain is far more severe and tends to affect the joints and the postorbital space, which is not true in influenza. In *dengue* there is a leukopenia and a decrease of the polymorphonuclear leukocytes. Some writers give the pulse-rate as rapid, others as distinctly slowed.

There are also hemorrhages from the mucous membranes, principally of the gastro-intestinal tract, occasionally from the respiratory tract. The general absence of respiratory findings probably offers the best means of differentiation of dengue and influenza. Later there is a characteristic rash which spreads from the thumb over the dorsum of the hand, also from the great toe over the dorsum of the foot, and is particularly distributed about the joints, thence over the whole body, sometimes measles-like in character, at other times scarlatiniform. It is quite characteristic and offers further aid in differentiation.

Influenza may be confused with early typhoid in that very often the initial symptoms of typhoid are respiratory. Ordinarily, however, the more insidious onset of typhoid will rule out influenza. We must be on our guard, however, for the occasional case with an acute onset. After the lapse of forty-eight hours the diagnosis is easy, with a report on blood-culture or Widal reaction.

Influenza may be taken for an acute abdominal condition requiring surgical interference, and the surgeon should ever have this possibility in mind. J. Dubs reports that during the last gripe epidemic there were many cases in which either in the beginning of the disease or in its further course the symptoms distinctly suggested appendicitis. In some cases at the beginning of disease the abdominal symptoms appeared before the pulmonary. There were distinct local signs of appendicitis in the form of pain and mild superficial hyperesthesia. Disproportion of the temperature and pulse-rate (in influenza the pulse-rate is slow) and absence of leukocytosis are valuable points. Abdominal symptoms may appear later in the course of influenza. Here we must remember that neuritis of the intercostal nerve occurs quite frequently during the course of influenza. On the other hand, we may have, due to secondary invaders, actual cholecystitis, appendicitis, and peritonitis; the absence of vomiting and leukocytosis would tend to exclude some complications.

Much evidence has been adduced in favor of the theory that encephalitis lethargica and influenza are one and the same disease. It is not conclusive. Flexner, in a recent contribution

on this subject, says "that the pandemic of lethargic encephalitis of the second decade of the twentieth century is quite unprecedented in recorded medical history and is probably not merely an unusual nervous manifestation of epidemic influenza, but is rather an independent affection, etiologically considered to be compared in its specific nature with other definite pathologic entities such as typhoid fever, tuberculosis, poliomyelitis, and epidemic meningitis."

**Complications.**—The most important of the complications of influenza are the pulmonary, bronchopneumonia being by far the most common. Excluding the aforementioned fulminant type there are: the interstitial and lobular bronchopneumonias caused most usually by the *Streptococcus hemolyticus*, the bronchopneumonia caused by *Bacillus influenzae*, lobar pneumonias caused by the various types of pneumococci, and finally the pneumonias caused by bacillus of Friedländer, *Staphylococcus aureus*, *Streptococcus viridans*, and *Micrococcus catarrhalis*. Time and space does not permit detailed description of the various types. This case is illustrative of such complications.

**Case V.**—Female, age nineteen, single. Patient enters hospital with history of headache, backache, sore throat, cough (unproductive) for past two days; also some pain in the chest.

*Examination* at entrance shows conjunctivæ and pharynx injected, tonsils small, slightly reddened. No exudate over pharynx or tonsils, lungs generally negative, as also the heart. Tentative diagnosis, influenza. At the time of entrance temperature was 104° F., pulse-rate 130. On the day after entrance temperature dropped to 99° F., pulse-rate to 100, with little variation until the fifth day of the disease, when there was a sudden rise of both pulse and temperature, the temperature going as high as 106° F., and pulse to 130. White blood-count at entrance 4900. Four days after entrance, coincident with rise of temperature and pulse, 1600 per cubic millimeter.

At this time physical examination shows heart out to the left 12 cm., otherwise negative. There is definite bronchial

breathing and few moist râles, also bronchophony all over the right side of chest posterior. Examination of chest the next day showed harsh breath sounds on the upper portion on the right side of chest, on the left a few moist râles. Blood-pressure 120 systolic, 80 diastolic. One week after entrance the pulse-rate was 140, respiration 44, heart negative, percussion note dull in the left side of chest from the supraclavicular fossa, also posteriorly over the entire lower two-thirds. Here there was also tubular breath sounds and bronchophony, later on this day the heart showed signs of dilatation. On the following morning respiratory rate was 48, there was a marked cyanosis of lips and nail beds, also harshened breathing over the left side, many coarse râles on the right side. Pulse-rate 150, blood-pressure 128 systolic, 80 diastolic.

Re-examination of chest later in the day revealed wheezing sounds all over the right front of chest and left axillary region, tubular breathing low down, above the third rib; below this the breath sounds are almost normal, but very distant at times. Heart sounds strong, there is dulness over the left axilla, few crackles and wheezings can be heard over this area, very little cough. Patient died a few hours after this examination. Diagnosis: Bronchopneumonia and serofibrinous pleurisy left side. Blood-culture showed positive for streptococcus, complement fixation for tuberculosis negative, Wassermann negative, urine was positive for sugar, otherwise negative. The temperature throughout the course of the disease and the pulse-rate remained up until the time of death.

Postmortem examination revealed the following anatomic diagnosis: Bronchopneumonia upper lobe left lung. Serofibrinous pleurisy left side, local areas of bronchitis and bronchopneumonia right. Compensatory emphysema, apex of the left lung and large part of right lung and general congestion of the viscera. Microscopic: Gross examination of the lungs shows on the right upper lobe irregular areas about the size of a walnut, on section these areas are red and hemorrhagic, there are several areas in the upper part of the left lobe, the pleural surface everywhere is slightly roughened and hemorrhagic. Microscopic

examination of the lung shows the right upper lobe alveoli greatly dilated. There is a small area of bronchopneumonia in upper lobe of the left lung and without, the alveoli are filled with pink granular material, the walls are congested with fibrinous material, polymorphonuclears, leukocytes, and red cells. Everywhere there are many epithelial cells. The same findings can be made out in other portions of left lung. Cultures from the lung at postmortem show *Streptococcus viridans*.

**Case VI.**—Male, age thirty-four. Enters hospital with history of taking cold two days before, symptoms at this time not severe enough to cause much alarm, temperature then 99.4° F., patient remained up and continued his regular duties. One day before entrance to hospital affected with severe backache, also pains in extremities and headache. Throat was moderately sore. There was at this time the complaint of general dizziness. Temperature was 102° F. Patient still thought he had an ordinary cold and remained home. On the morning of entrance to hospital the temperature was 103° F., and patient experienced distinct chill, followed by sweat, after which he felt much better. Now complains of headache, backache, general burning of eyes, and very slight scratchy sore throat; there is a slight cough which is not productive. Appetite good, no digestive disturbance, bowels regular. Examination on entrance shows a slight congestion of the conjunctiva, soft palate, and pharynx. Lungs show nothing, heart negative, abdomen shows slight tenderness in the upper portion. Diagnosis: Influenza.

Next day the urine was negative, white blood-count 7400, temperature at entrance 101° F., pulse 85. Shortly after temperature rose to 104° F. and the pulse to 87. The day following entrance the temperature dropped to 99.4° F. and the pulse to 65, at about which level both continued until the fifth day. The third day after entrance a few crackling râles were made out at the right base, also on the left; no other physical findings of chest. Five days after entrance patient had severe chill, temperature rapidly rose to 103° F. and pulse-rate to 110. Cough has become more productive, with mucopurulent sputum. Slight

cyanosis in evidence about the lips, ears, nails, and over the chest, no râles at this time, but a slight suggestion of increased whispered and voice sounds over the lower margin of the right base. Respirations rose to 42. Sputum became bloody and there was suggestion of tubular breathing over the right base, no râles. On the following day there were coarse râles over the right upper portion of the chest anterior, also diminished resonance, tubular breathing, and bronchophony over the right base. At this time patient was given 100 c.c. antipneumococcus serum, and later on the same day 50 c.c., both intravenously. On the following day the temperature dropped to 100.5° F. and pulse to 90. Despite the temperature and the pulse changes there was no appreciable change noted in the patient's condition or physical findings of the chest. Blood-pressure at this time 104 systolic, 64 diastolic. Physical examination on the following day showed an area of tubular breathing below the left scapula about mid-back, also bronchophony. There is a similar area on the right side with the same findings, râles are heard everywhere except at the apices, the pulse is weak and dicrotic. Patient is troubled with constant cough accompanied by serous liquid blood-stains.

Further physical examination: Examination on the following day shows same findings, with the exception of diffuse râles both sides, nails are more cyanotic, and the color is distinctly bad over trunk and extremities. At this time respirations are 42, pulse 132, and the temperature 104° F.; there is a progressive increase in the pulse-rate, also temperature, which continues until next day, when the temperature reaches maximum of 108° F., pulse 160; respiration at this time 48. The patient grows progressively weaker and there are no breath sounds below the fifth interspace of both axillæ. The leukocyte count never reached above 7000 and at the time of death, coinciding with the previous observations, was 5900. Polymorphonuclears predominating. Throat culture shows *Staphylococcus albus* and *pneumococcus*. Blood-culture negative, complement fixation for tuberculosis negative. It is noteworthy that on the last day of the disease with the maximum temperature of 108° F. the white blood-cell count was 2100. Autopsy was refused. Clinical

diagnosis being influenza followed by bronchopneumonia, right and left, and acute pharyngitis.,

**Complications.**—Bronchitis complicates nearly all cases of influenza and pleurisy is quite frequent, especially with pneumonias due to pneumococcus. Empyema, particularly with *Streptococcus hemolyticus*, often occurs. Influenza has a definite effect on the myocardium which may persist for months after recovery. Endocardial complications are rather rare. There is definite lowered resistance of the nasopharynx, sinuses, and internal ear during influenza, so that otitis media and sinusitis are very frequent complications; any of the secondary invaders aforementioned giving rise to these conditions. Meningitis, the etiologic agent being any of the secondary invaders, is occasionally met with.

**Sequelæ.**—Attention has been called to the damage to the myocardium during an attack the effects of which persist sometimes for several months. These individuals become short of breath on the slightest exertion, suffer with palpitation, and may have either bradycardia or tachycardia. Chronic asthenia is of very frequent occurrence, due probably to the effect of the influenzal virus on the adrenals. The very frequent hypotensions met with since the recent epidemic of influenza may find their explanation here. The subject offers a fertile field for conjecture. However, all of us meet many individuals, some of whom have had very mild and fleeting attacks of influenza characterized by sore throat, possibly a rise of one degree of temperature with the total duration of two or three days or less; almost invalided for periods of months after such an attack. Fatigability is a very marked symptom in these patients, blood-pressure is low, systolic often below 100. The slightest effort, mental or physical, brings about profound tiring. Many, and I think properly so, have ascribed this syndrome to the effect of influenza virus on the adrenals. At postmortem definite degenerative changes have been found in the medulla of the adrenal gland of patients dying with influenza.

Chronic bronchitis and bronchiectasis also occur with varied



frequency. In this connection it is important to emphasize the difficulty which has frequently arisen in differentiating possible postinfluenzal conditions of the lungs and tuberculosis. One may very easily be mistaken for the other. The history of an attack of influenza should put us on our guard. These patients complain of being easily tired, poor appetite, dry, persistent cough, and there may be slight evening rise of temperature. The physical examination shows general pallor. The lungs may show small areas of hyporesonance with feeble breath sounds, bronchovesicular in character and possibly crepitant râles, sometimes heard only after expiratory cough. The lower right lobe is most often affected, although I have observed the condition at one or both apices. Many of these cases show roentgenograms of the chest with triangular areas of increased mottling at the periphery of the lung and extending to the hilus in that part which yields signs. Before this condition was called attention to many roentgenologists misinterpreted the plates of these cases as indicating active tuberculosis. These cases generally tend to recover in from two to three months. In the present state of our knowledge tuberculosis can only be excluded by persistent absence of the tubercle bacilli.

Encephalitis lethargica has been thought to be a sequel or a different form of influenza. The weight of evidence is against the validity of this assumption.

**Prognosis.**—Uncomplicated, non-fulminant types of influenza ordinarily recover. Signs of developing pneumonia, marked cyanosis, bloody expectoration, and pulmonary edema are unfavorable symptoms. Perhaps pneumococcus pneumonia cases offer a better prognosis than the types caused by other secondary invaders. Influenza complicated by pregnancy offers a bad prognosis, abortion usually occurs, and if pneumonia ensues the prognosis is almost invariably fatal.

**Treatment.**—1. *Prophylactic.*—All patients with influenza should be isolated. The question of whether or not they should be hospitalized I believe should be answered in the negative, this on account of the greater danger of contact with secondary invaders in the hospital. If sent to the hospital, they should



have individual rooms and preferably a special nurse. Cases of influenza should not be treated in a ward. This was very forcibly demonstrated during the World War by very careful bacteriologic observation. Many convalescing from influenza who showed the absence of the usual secondary pneumonia-producing invaders were later taken with pneumonia of the identical type of a fellow patient in an adjoining bed. The individual should be provided with either sputum cup or gauze for expectoration, and these should be disposed of in the usual manner.

2. *General Management.*—The room should be light and well ventilated and temperature should not be over 60° F.; absolute rest in bed is necessary throughout the attack, no matter how mild, and for at least one week after the temperature has reached normal, this on account of the danger of secondary complications. Soft diet, high fluid intake except when contraindicated by edema or other cause. Hydrotherapy in the form of sponging when high temperature causes restlessness or other untoward symptoms is indicated.

*Specific Treatment.*—Up to the present antiserum for *Bacterium pneumosintes* is not available, but experiments tend to show that the production of specific anti-influenzal serum is possible. Until it becomes available nothing can be done to influence the disease itself. True, in epidemics the possibility of convalescent serum suggests itself. This has been very effective when tried. However, the average case, offering a good prognosis, does not need it, besides the preparation of it is very laborious and complicated. For the fulminant complicated cases of influenza convalescent serum offers the best therapy.

Simici reports excellent results from the daily subcutaneous or intramuscular injection of 10 to 20 c.c. of convalescent blood; this treatment was tried on 24 patients suffering from a grave form of influenza, and of these, 20 recovered. In nearly all the temperature was lowered to some extent by the injection, its action on bronchopulmonary complications was less definite. Keegan obtained encouraging results by the intravenous use of convalescent serum during the pandemic of 1918.

*Drug Therapy.*—For the most part the treatment of uncomplicated influenza resolves itself in the treatment of symptoms, this in the form of local applications to the throat, argyrol 25 per cent. solution, mercurochrome 3 to 5 per cent., and cracked ice. Dover's powder,  $7\frac{1}{2}$  gr., tends to promote rest, allay cough, and to increase the tracheobronchial secretions. The cough should be controlled as much as possible on account of the danger of aspiration of secondary organisms present in the throat. Usually after a fit of coughing the patient takes very deep inspirations which offers excellent opportunity for aspirating "his own spray," this, of course, if he be in a reclining position.

For the control of pain and general toxic symptoms some form of salicylate, preferably aspirin in conjunction with codein, is to be recommended. In our experience the use of alcohol in the form of whisky seems to have had a distinct beneficial effect. The use of vaccines containing mixtures of the usual secondary invaders is recommended during the course of epidemics toward the end of preventing the complications caused by these organisms.

*Complications.*—Pneumococcus serum, Type 1, for this type of pneumonia should be the routine, 50 to 100 c.c. being given as often as every twelve hours until the course of the pneumonia is favorably influenced. Types 2, 3, and 4 pneumococci have not up to the present given rise to specific antiserum. Conner reports on the intravenous use at the New York Hospital of free antibody solutions prepared according to the method of Huntoon. Routine doses average 50 c.c. for men and 25 c.c. for women; after an interval of twenty-five minutes to one hour there is a chill followed by rapid rise of temperature; very soon this falls and may reach normal in a few hours. This is accompanied by profuse sweating, marked slowing of the pulse, and improvement in all subjective symptoms. In 90 cases of pneumococcus pneumonia the mortality was 14.6 per cent., against 32.2 per cent. average of the hospital for the previous twenty years. Mortality in Type 1 was 13 per cent., Type 2, 22 per cent., Type 3, 33 per cent., and Type 4, 4 per cent. Cole's statistics

at the Rockefeller Institute show that when serum is not used the mortality for Type 1 is 25 to 30 per cent., Type 2, 20 to 30 per cent., Type 3, 35 to 50 per cent., Type 4, 14 to 20 per cent. Besides the specific antibodies group, protective substances of less specific nature may serve to explain the favorable results obtained with the antibody solutions.

Cecil reports a difference in the mortality rate for Type 1 pneumococcus cases of 10 per cent. in cases treated with a modified antipneumococcus serum, consisting of a watery solution of the immune bodies originally contained in polyvalent antipneumococcus serum and known as pneumococcus antibody solution, the mortality for the treated cases being 13.4 per cent., as compared with 23.4 per cent. for the untreated cases. There was a difference of 12 per cent., 5 per cent., and 7 per cent. less for the treated cases of Types 2, 3, and 4 respectively, as compared with the untreated; 50 to 100 c.c. of the antibody solution is administered intravenously once or twice daily. This is followed by a violent chill and rise of temperature, which rapidly falls. He says that contraindications to its use are: (1) Complicating severe systemic disease, cardiac, renal, or vascular; (2) exhaustion due to the infection in cases seen late in the disease, and (3) pneumonia in the aged.

In addition to whatever specific antibodies may be present in these solutions, their action definitely partakes of the reaction following the injection of foreign proteins. In fact, very favorable results have been reported with the use of proteoses and typhoid vaccines intravenously, all giving rise to sharp chills, fever, leukocytosis, followed by sweating and general improvement of subjective symptoms. Such treatment should be reserved for sthenic cases, and if used should be used as early in the disease as possible.

The treatment of pneumonia by specific vaccine when the offending organism can be isolated or by mixed vaccines is held in favorable esteem by several competent clinicians. Theoretically, of course, they are not indicated. It is quite possible, however, that they may give rise to antibodies at the site of injection and thus favorably influence the disease. The leuko-

cytosis following their administration probably is produced by their foreign protein properties.

*Quinin.*—Many authors report the favorable influence of quinin on the course of pneumonia. It is well to know that quinin derivatives, especially ethylhydrocuprein, in rather large dilutions is bactericidal for pneumococcus. This is indeed a toxic drug and its value has been questioned by the findings of Chesney, who investigated it in the treatment of pneumococcus pneumonia at the Rockefeller Institute.

*Tracheal Medication.*—This, in the form of insufflations in influenza, is to be discouraged on account of the danger of producing lowered resistance of the mucous membranes by the preparations used; also on account of the danger of aspiration of infected material into the bronchioles and alveoli. Local treatment in the nose, nasopharynx, and pharynx in the form of argyrol 25 per cent. or mercurochrome 3 to 5 per cent. is recommended.

*Digitalis* therapy should be begun at the first sign of pneumonia, also in severe bronchitis. A standardized tincture is the preparation of choice and should be so administered that the calculated dose per body weight, namely, 15 c.c. per 100 pounds body weight, should be given within three or four days. In emergencies arising out of heart failure caffein sodium benzoate or camphorated oil intramuscularly are to be recommended. The exact effect of camphorated oil on the pneumonia or its course other than the stimulative effect on the heart is an open question. Many report favorable results by its continuous use through the course of pneumonia. Intravenous glucose, 5 to 10 per cent. solution of 100 to 200 c.c., tends to combat acidosis, furnishes food, and where there is no contraindication in the form of fluid retention or heart failure its use may combat the edema of the lungs in the fulminant cases described above; this on account of its osmotic and diuretic effects. Other symptoms are to be treated as they arise.

*After-treatment.*—All patients should routinely be kept in bed for at least one week after subsidence of temperature. Ordinary tonics, in the form of iron, strychnin, arsenic, are to

be given in the asthenic cases. Suprarenal substance whole gland, gr. v three times a day, seems to have a distinct value in cases showing fatigability, general asthenia, and low blood-pressure following influenza.

Complications of a surgical nature are to be handled by the surgeon. The technic need not be described here.

*Prophylactic Inoculation.*—The prevention of influenza by vaccine has up to the present not been possible. However, vaccines of the *Bacterium pneumosintes*, experimentally, have given rise to protection. The prospects in this direction are very promising for the ultimate preparation of an effective vaccine. The use of mixed vaccines so prevalent during the epidemic is to be commended on the grounds of possible prevention of secondary infections. Such vaccines contain the *Micrococcus catarrhalis*, three types of pneumococci streptococcus, and *Staphylococcus aureus*. We would emphasize higher dosage in the administration of these, also conservatism in drawing deductions as to the value of their use. Whenever a vaccine is used, before deciding on its effectiveness or infectiveness we should, as in the case of administering any therapeutic agent, determine as best we can just what it has accomplished. To this end serologic tests for the presence of antibodies should be carried out routinely at the end of vaccination or often during the course of vaccine therapy.

#### BIBLIOGRAPHY

George Baehr and Leo Loewe, *Arch. Int. Med.*, 30, 307, September 15, 1922.

Peter K. Olitsky and Frederick L. Gates, *Jour. Exper. Med.*, 36, 501, November 1, 1922.

Ludwig Petschacher, *Beitr. z. Klin. d. Tuberk.*, Berlin, 54, 372, March 12, 1923.

Oliver H. Stansfield, *Boston Med. and Surg. Jour.*, 188, 734, May 10, 1923.

Mervyn H. Gordon, *Brit. Med. Jour.*, London, p. 299, August 19, 1922.

James McIntosh, *Brit. Med. Jour.*, London, p. 303, August 19, 1922.

H. Kadysz, *Polska gaz. lek.*, Cracow, 1, 626, July 30, 1922.

W. H. Wynn, *Lancet*, London, 203, 493, September 2, 1922.

S. Yabe, *Kitasato Arch. Exper. Med.*, Tokyo, 5, 67, August 11, 1922.

C. F. T. East, *Brit. Med. Jour.*, London, p. 1117, December 9, 1922.

G. Elkeles, *Klin. Wehnschr.*, Berlin, 1, 2421, December 2, 1922.

- Peter K. Olitsky and Frederick L. Gates, *Jour. Exper. Med.*, 37, 471, April, 1, 1923.
- Guisepppe Belloni, *Riforma Med.*, Naples, 39, 198, February 26, 1923.
- Arthur L. Bloomfield, *Bull. Johns Hopkins Hosp.*, 33, 172, May, 1922.
- J. Dubs, *Schweiz. med. Wchnschr.*, 52, 363, Basel, April 13, 1922.
- D. Oelsnitz and Colle, *Bull. et mém. Soc. med. d. hôp. de Paris*, 38, 822, June 1, 1922.
- Spiro Livierato, *Presse med.*, Paris, 30, 500, June 10, 1922.
- Ambrose W. Owen, *Brit. Med. Jour.*, London, p. 946, June 17, 1922.
- Russell L. Cecil, *Amer. Jour. Med. Sci.*, 164, 58, July, 1922.
- S. W. Patterson and F. E. Williams, *Lancet*, London, 203, 806, October 14, 1922.
- Andrew Garvie, *Glasgow Med. Jour.*, 98, 232, October, 1922.
- Robert L. Levy, *Arch. Int. Med.*, 32, 359, Spetember 15, 1923.
- Peter K. Olitsky and Frederick Gates, *Jour. Exper. Med.*, 36, 685, December 1, 1922.
- Lewis A. Conner, *Amer. Jour. Med. Sci.*, 164, 832, December, 1922.
- A. Bloomfield and G. A. Harrop, Jr., *Bull. Johns Hopkins Hosp.*, vol. 30, January, 1919.
- McCallum, *Text-book of Pathology*, Saunders Co., 1920.
- A. M. Chesney, *Arch. Int. Med.*, 1917, xix, 611 (with Moore).
- Hans Zinsser, *Med.*, 1, 213, August, 1922.

## CLINIC OF DR. J. CURTIS LYTER

ST. ANTHONY'S HOSPITAL

### MULTIPLE ADENOCARCINOMA OF THE BRAIN

FOR our first lesson this morning I desire to delineate to you a case possessing many interesting and instructive features. The gentleman to whom the brain before us belonged was a patient in this hospital on the service of Dr. McKay eight months ago. At that time he was operated upon for the relief of a rectal cancer, the operation being a colostomy. From this operation he nicely recovered and was in a very satisfactory condition until three months ago, when the syndrome terminating in his death developed.

Beginning about three months before his death this patient noticed a gradually increasing weakness with some stiffness in the muscles of the left arm and leg, rendering movement of these members difficult and cumbersome and finally impossible. Associated with this symptom there was some headache of a dull, boring character, some impairment of memory, and frequent attacks of nausea, vomiting, and dizziness. In a state of left spastic hemiplegia the patient entered my service in this hospital six weeks before his death. At that time and until his death he presented the picture of a spastic, slowly progressive, left hemiplegia, with a rapidly progressive and finally complete impairment of the psychic state. There was very little change in the reflex phenomena during these six weeks, but the mental state progressed into a coma, in which the patient died. Upon our first examination the following features were observed: The entire left side of the body and face revealed a muscular stiffness which was easily demonstrated; there was a pronounced tremor of the tongue, lips, and extended fingers; the protruded tongue deviated distinctly to the left; there was a rather pro-

nounced stiffness of the left facial muscles of expression; the left palpebral fissure was wider than the right; the triceps reflexes were present, equal, moderate; the biceps were present, the left being much more lively than the right. The same was true of the radial and ulnar reflexes. There was a distinct Chaddock's wrist sign on the right, but none on the left. The epigastric and abdominal reflexes were present, equal, and lively.

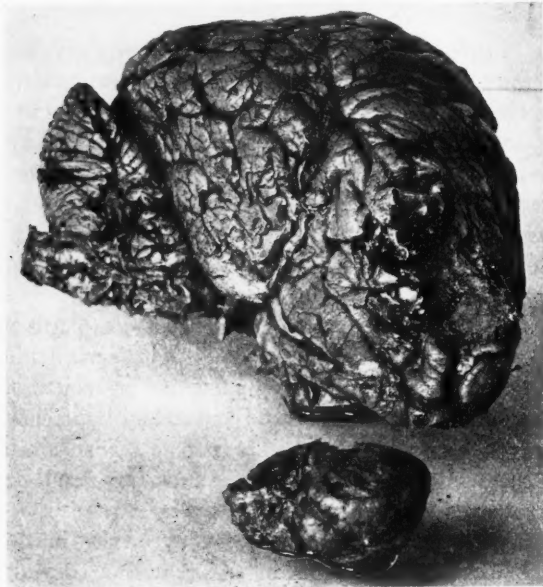


Fig. 268.—Photograph of the brain revealing the site of the tumor in the right frontal lobe and the enucleated tumor.

The left cremasteric was much more lively than the right. The patellars and Achilles were present and lively, the left being much more so than the right. There were Babinski and Chaddock signs on the left and a more pronounced Chaddock on the right. There were no Gordon or Oppenheim signs. The cutaneous sensations to pain, touch, and temperature were apparently normal, although the patient's mental state rendered the



examination rather difficult. Ophthalmoscopic examination revealed a moderate, double choked disk. A complete general examination revealed nothing of importance except an advanced carcinoma of the rectum. The examination of the urine, blood, and spinal fluid failed to demonstrate anything of clinical importance.

The features of this case which impress one immediately are these: A known carcinoma of the rectum existing for eight or ten months; an insidious, spastic, progressive left hemiplegia;

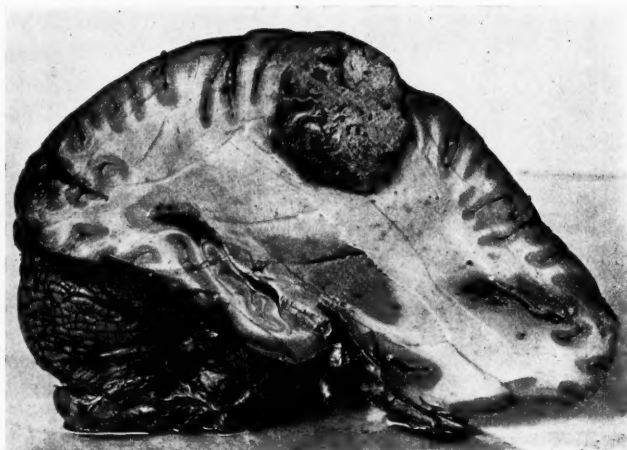


Fig. 269.—A sagittal section of the brain revealing the tumor in the right motor area.

continuous frontal headaches; attacks of nausea and vomiting and a rapidly declining mentality. The hemiplegia, headache, and attacks of nausea and vomiting are sufficient evidence upon which to base a diagnosis of cerebral tumor, and since one knows of the presence of a rectal carcinoma, the tumor could only be considered metastatic. Years ago I was taught by that great neurologist, to whom I have always been greatly devoted, Dr. C. G. Chaddock, that an insidious hemiplegia has for its etiology a cerebral tumor unless some other cause can be definitely demonstrated. A clinical diagnosis of metastatic carcinoma in the

right motor area was made. The patient died in the state of coma after being in the hospital for about six weeks. At no time during this observation was there any evidence of local or general convulsions. An autopsy of the brain alone was obtained, and we have that organ before us for study. You are able to see a tumor in the right frontal lobe and a second one in the right motor area. The larger tumor is situated in the frontal lobe.



Fig. 270.—Demonstrating the technic and the earliest manifestation of Chaddock's phenomenon. Case of encephalitis lethargica.

I have here under the microscope some stained sections of each tumor and you will recognize each tumor as an adenocarcinoma, and in one section you can easily identify some intestinal glands. From this finding alone we can be very positive concerning the origin of this tumor. A very interesting feature of the autopsy is the finding of multiple tumors which was not suggested by the clinical study. Numerous sections were made through each

hemisphere and cerebellum in search of other tumors, but none were found. We can rest fairly well satisfied, then, that there were only two metastatic tumors.

There are several interesting features to this case and we will study each one individually for a few moments. The first feature is the increased reflexes noted generally on the left side, and the absence of any disturbance of sensation. There was also a positive Babinski and Chaddock on the left. These findings, if they indicate anything at all, indicate a lesion in the right motor area. Besides these reflex findings we have the positive Chaddock at the right ankle and right wrist. These phenomena described by our venerated teacher, Dr. Chaddock, are some of the most valuable of all the reflexes you will find in the various text-books. It is rare, however, to see a clinician who has taught himself the technic of producing Chaddock's external malleolar sign, and extremely rare to find one who can produce and interpret his wrist sign. These phenomena are not difficult of production, and when present indicate physical changes in either the crossed or homolateral motor tracts. To produce the wrist sign one places the thumb of his left hand in the palm of the patient's hand, and with the fingers to the back of the hand holds the hand rather firmly, simultaneously obtaining a complete relaxation of the muscles of the forearm by diverting his attention. At this time some stimulation by means of scratching with the point of a nail file, pin, or other sharp instrument the thenar, hypothenar eminence, and the adjacent palmar surface of the wrist is applied. A positive reaction begins with a contraction of the flexor carpi radialis muscle and may consist of this contraction alone, but, as a rule it is followed by a contraction of the thenar and hypothenar muscles, and finally a contraction of the entire flexor group, producing a distinct palmar flexion of the hand upon the wrist. I have seen the phenomenon result from stimulation applied to the dorsum of the hand or the forearm. The presence of this phenomenon indicates a physical change in the motor pathways above the cervical enlargement of the cord or in the motor cortex. Chaddock's wrist sign is usually present on the side

corresponding with the cerebral lesion and indicates changes on the homolateral fibers. The external malleolar sign described years ago by Chaddock is produced by stimulating the skin along the external plantar border, around the external malleolus, along the external aspect of the leg to the knee, and at times in rather extensive cortical lesion I have been able to elicit the phenomenon by applying stimulation to the internal aspect of



Fig. 271.—A moderate manifestation of Chaddock's phenomenon as noted at the wrist.

the arm. In diagnostic significance this phenomenon is similar to those of Babinski, Gordon, and Oppenheim, and I am quite positive that it is a more delicate finding and occurs regularly in the destructive processes affecting the upper motor neuron. The reaction to the stimulation is positive when one observes a fanning of the toes or a straightening and fanning of the toes with a dorsal flexion of the great toe, as is observed in the Babin-

ski reflex. In the maximum reaction one is able to observe the above response in addition to a sudden contraction of the hamstring and anterior tibial group of muscles.

A second phase of this case which should be closely studied is that of increased intracranial pressure. This gentleman complained of dizziness, nausea, vomiting, severe headaches, and mental deterioration. Along with this, the ophthalmoscope revealed a double optic neuritis or choked disk. These are the



Fig. 272.—Rather marked positive Chaddock's phenomenon noted in the case under discussion.

positive evidences of increased intracranial pressure. There are many interesting aspects of increased intracranial pressure as the result of cerebral tumors, especially as regards the anatomic division of the cranial cavity by the falx and tentorium into three more or less separate and independent cavities. The size, nature, rapidity of growth, and location of the tumor and especially the latter may all play a certain part in increasing the intracranial pressure.

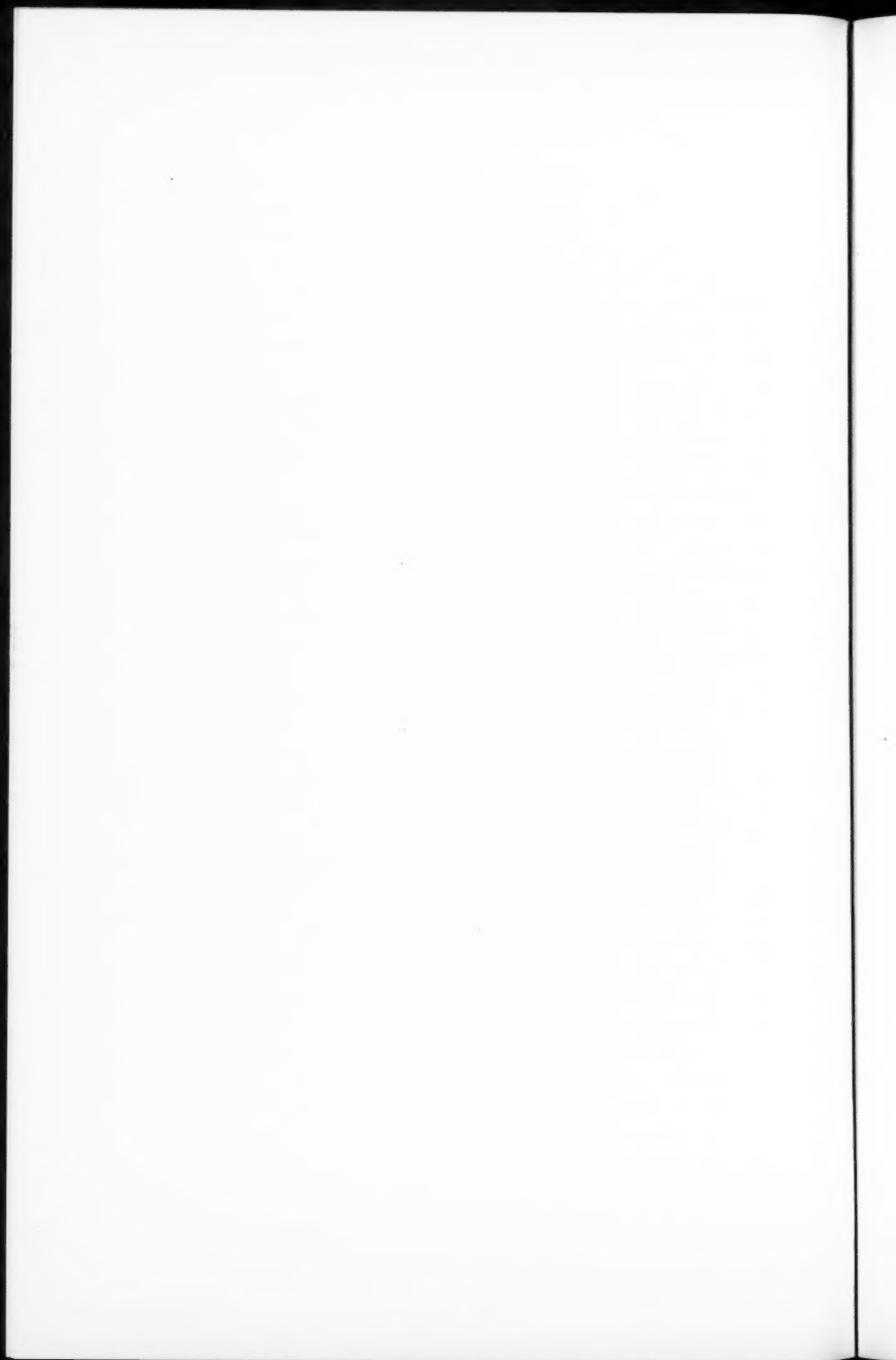
Observation of these cases seems to prove that a tumor which

grows rapidly is more frequently accompanied by symptoms of increased intracranial pressure than one of slow growth. Probably the cranial contents are capable of adapting themselves to some extent by a process of compensation to a gradually increasing pressure, with the result that a disturbance of function is not so apt to occur in the slowly growing as in the more rapidly growing tumors. Again, it should be remembered that those tumors which, while increasing in size, destroy brain tissue, do not, as a rule, produce the increased cranial pressure so frequently seen in those tumors which by their very nature displace brain substance in the course of their growth. Our patient had two tumors of the rapidly growing kind, and this in itself is sufficient to account for the rapid and progressive course of those symptoms of increasing intracranial pressure.

The third and last phase I wish to discuss with you is that of the mental symptoms and multiplicity of the tumors. First, it will be noted that a clinical diagnosis of a tumor in the right motor area was made, while at the autopsy a tumor in the right frontal lobe in addition to the one in the right motor area was found. It was not difficult to locate and classify the tumor in the motor area when one gave careful consideration to the clinical history and the physical findings, but I am frank to admit that we gave no thought to the presence of an additional tumor in the frontal lobe. Taking a careful retrospection of the case now, however, I am really provoked that this tumor was not also recognized. The mental condition of the patient changed so rapidly and coma occurred so early after the onset of the other symptoms of increasing intracranial pressure, that one should have recognized in this the result of a tumor situated in the frontal lobe.

Some degree of mental impairment is probably seen in a large proportion of the brain tumors wherever located, but there is nothing characteristic or distinctive about the mental symptoms which are associated with brain tumors. Two groups are especially recognizable in relation to the mode of production of the symptoms. In the first group are those mental disturbances due to destruction of the brain tissue. Many observa-

tions have been reported which seem to prove that tumors of the frontal and temporal lobes and of the corpus callosum are accompanied by mental disturbances. The mental changes may be slight in degree and only apparent, as an alteration of temperament or character, discernible by one who knows the patient intimately. On the other hand, the abnormality may be very outspoken; pronounced apathy, faulty judgment, failing interest in conditions both personal and general, the complete loss of sense of responsibility and impairment of memory are at times observed. From the diagnostic standpoint there is nothing in the abnormal mental state characteristic of a frontal lobe tumor, since, as indicated, there may be such great variations in the mental condition. The early and progressive mental symptoms in the presence of other evidence of cerebral tumor should incline one to locate the tumor in the frontal lobe. Certainly in right-handed people the presence of motor aphasia in conjunction with the mental and other signs of tumor would indicate a tumor in the region of Broca's area on the left.





## MULTIPLE EMBOLI

THE second case for study, gentlemen, is that of a painter, fifty-four years of age, who entered the medical service on November 20, 1920, being referred by Dr. Gregory Miller. His illness began on November 1st, at which time he suffered an acute tonsillitis. Following the acute tonsillar infection he noticed an inability to resume his former duties because of a lack of strength, and about two weeks after the infection a rather pronounced and unprovoked dyspnea was manifest. Associated with this there was some precordial discomfort and a slight and unproductive cough. He entered the medical service here at this time, and upon examination we found a very muscular and well-nourished gentleman, 6 feet, 3 inches tall, weighing 230 pounds. The salient positive findings as discovered during a complete general examination were as follows: The heart rate was 120 per minute. The pulses were equal, regular, synchronous, and of a fair volume. There was no palpable sclerosis in the arterial walls. The heart apex impulse was in the left fifth interspace at the midclavicular line, being well localized and of moderate force. There were no precordial retractions, thrills, or shocks. The left border of the heart was 2 cm. external to the midclavicular line at the fifth interspace. The right border was 4 cm. from the midsternal line at the right fourth interspace. The line of cardiac dulness at the left second, third, and fourth interspaces was displaced upward and outward. Upon auscultation one could hear a blowing, systolic murmur at the apex transmitted to the left axilla and over the precordium. Slightly above the apex there was present a presystolic rumble. The pulmonic second sound was definitely accentuated. The patient being placed in the left lateral position, the cardiac dulness moved 4 cm. to the left at the fifth interspace. In this position the auscultatory signs were similar to those described in the reclining position. Other than these no abnormal findings about the cardiovascular system could be

elicited. An examination of the respiratory system proved the presence of numerous inspiratory, crepitant râles throughout each lung posteriorly below the scapular spines. Otherwise the respiratory examination revealed no positive findings. The urine contained a rather large trace of albumin, numerous red blood-cells, casts of the hyaline and granular type, and a moderate number of leukocytes. The blood contained 14,600 leukocytes per cubic millimeter, of which 84 per cent. were polymorphonuclears. A number of blood and urine cultures gave negative results. The temperature varied from 101° to 102.5° F., being of a distinct, irregular type. With these findings a diagnosis of infective endocarditis and acute nephritis was made, and the usual treatment for these conditions instituted. The patient's condition was considered satisfactory until 4 A. M. on December 6th when there appeared very suddenly a severe, cramping pain in the left foot, leg, and thigh. Associated with this severe pain was a pronounced cramp in the gastrocnemius and soleus muscles. The intern at once ordered morphin,  $\frac{1}{2}$  grain hypodermically, for the patient, but this rendered very little relief. I saw the gentleman at 7.30 A. M. and observed the following signs: The entire left leg and foot were in a general, tonic, muscular spasm, the leg being extended and the foot in a state of dorsal flexion. There was complete dermal anesthesia over the lower third of the thigh and the entire leg and foot. The superficial veins were entirely empty and no arterial pulsation could be found. The leg and foot were cold and dry. At this time the patient complained bitterly of pain throughout the leg and foot, and a second hypodermic of morphin,  $\frac{1}{2}$  grain, was given, and again no relief was obtained. A diagnosis of embolism of the left femoral artery was made and a watch for the early signs of gangrene begun. At about noontime of the same day the pain entirely subsided and the muscles which were so spastic became completely flaccid. On December 7th the gangrene of the toes had begun and it progressed until, on the 13th, the line of demarcation about the middle of the thigh was complete. At this time amputation was made by Dr. H. S. McKay, and the stump healed nicely. We should not pass over the syndrome

just delineated without some study of some of the features which to me were most impressive. The severe pain in the leg, with complete dermal anesthesia, seems to me to prove that the sensory cutaneous nerve endings were destroyed many hours before the destruction of the motor endings. The destruction was, of course, due to starvation and probably the accumulation of certain toxic substances secondary to the cessation of circulation locally. When the motor endings were destroyed, probably by the same agents several hours later, the boring pain disappeared and the involved muscles became flaccid. The observation may have great clinical value in that it might prove the greater vulnerability of the sensory nerve endings to toxic substances and circulatory changes. I might ask you, gentlemen, if you do not find in your patients suffering with chronic infections and intoxications many pains, paresthesia, and other discomforts which can only be explained upon the basis of the action of toxic substances upon the sensory nerve endings. These pains vary greatly from day to day in character and location. Again I might ask you to explain the many pains and other discomforts described to you by the patient suffering with arteriosclerosis, cardiac inefficiency, or edema. The explanation of these various sensations in the extremities especially rests upon the effect of the disturbed circulation upon the sensory nerves and their endings.

Following the amputation this patient seemed to progress satisfactorily until the night of February 14th, when suddenly there appeared a severe pain in the lower right chest. The pain was most agonizing, respiration difficult, skin cold and moist, and the general picture of shock was marked. The pulse was 140, but regular and of fair volume, and the patient coughed and expectorated 1 or 2 ounces of bright red, frothy blood. One could hear upon examination of the lungs a pleural friction rub in the right midaxillary line at the sixth rib. Over an area at this point there could be heard numerous inspiratory, crepitant râles and altered respiratory sounds. After several hours the patient's condition became more satisfactory and signs of consolidation appeared over the area described. The cough con-

tinued, and after a few days was productive of a sanguinopurulent sputum. At this time the physical signs of consolidation gave way to the signs of cavitation. An x-ray plate, which you are able to study, was taken of the chest, and you will ex-



Fig. 273.—Flat plate of the chest revealing the large cavity in the right lower lobe.

perience no difficulty in convincing yourself of the presence of a large cavity in the lower lobe of the right lung. A second plate taken four weeks later shows the cavity absent. The diagnosis made at the onset of this new syndrome was a right pulmonary

embolism, and I believe we will all agree that the recovery was quite remarkable and out of the ordinary.

Very strange as it may seem to relate, the endocarditis and acute nephritis subsided under continuous treatment, and the

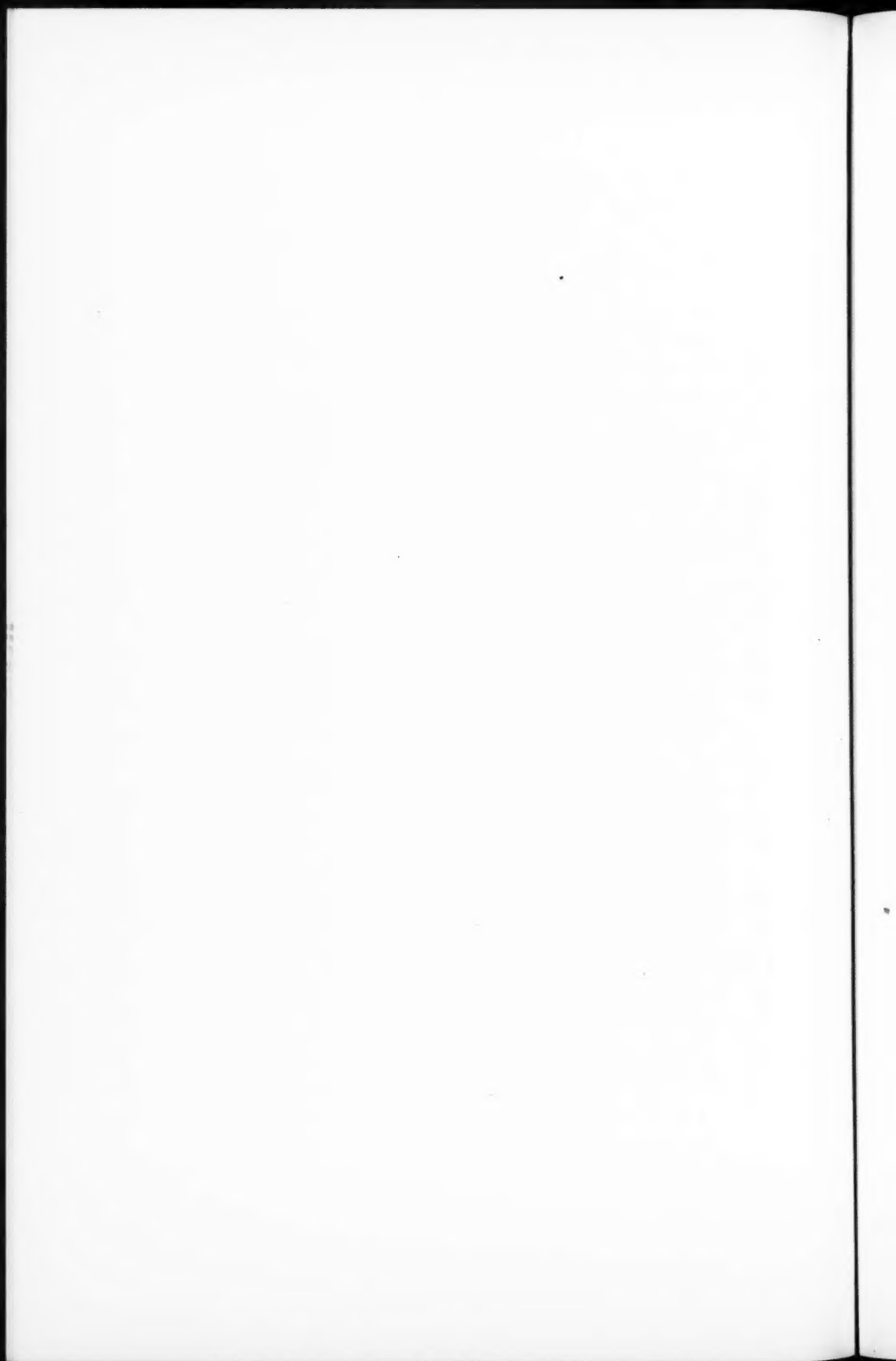


Fig. 274.—x-Ray plate revealing the absence of the cavity at the time of discharge.

patient left the hospital on April 4, 1921 feeling well. I did not see or hear from him again until on April 27th his son called at 11 A. M. stating that his father had been taken very suddenly with a most intense pain in the abdomen, nausea, and vomiting.

I called one of my colleagues, Dr. Fred Warner, and asked him to see the patient, as it was impossible for me to see him for several hours. Upon arriving at the patient's bedside Dr. Warner found him in intense pain, vomiting, with a cold and moist skin, pulse 140 per minute, obstinate constipation, and marked abdominal distention. Three hypodermics of morphin, each containing  $\frac{1}{2}$  grain, were given within two hours, but afforded no relief from the pain. I saw him about five hours after the onset of the pain, which he described as agonizing over the entire abdomen, but being more severe over the right half. The pulse at this time was 160 per minute, small, and not well sustained. The patient appeared to be in a profound shock with cold, moist skin of an ashy color. The abdomen was markedly distended and no borborygmi could be heard. The bowels remained obstinately constipated. A diagnosis of thrombosis of the superior mesenteric artery was made and the family advised of the hopelessness of the situation. The patient died twenty-one hours after the onset and an autopsy upon the abdomen alone was granted. At the autopsy the liver, spleen, and stomach were found to have a normal appearance; the kidneys were rather large, the capsules slightly adhered, and the anatomic markings rather pronounced. The important finding was that in association with the intestine. There was no evidence of gross intestinal obstruction, as from a hernia, volvulus, or intussusception. The entire small intestine, except the upper one-third of the duodenum, was entirely gangrenous. The cecum, ascending, and right half of the transverse colon were likewise gangrenous. The area of anastomosis between the inferior pancreaticoduodenal artery and the superior pancreaticoduodenal artery was purple in color. Finally, partial gangrene was observed over the area of anastomosis between the middle colic branch of the superior mesenteric and left colic branch of the inferior mesenteric. Upon dissecting out the superior mesenteric artery there was found a pronounced thrombosis extending from its origin to its primary branches. The diagnosis of thrombosis of the superior mesenteric artery was made upon a knowledge of a focus for emboli, as in this case

the emboli were probably formed in the left auricle as result of mitral stenosis and insufficiency. The fact that the blood-cultures were negative upon several occasions would seem to exclude the possibility of pronounced ulcerative endocarditis with bacterial emboli. The second point in the discussion of thrombosis of the superior mesenteric artery is the suddenness with which the pain appears, its intensely agonizing character, and its distribution over the entire abdomen, with a tendency to greater severity over the right half. The pain is continuous and is associated with the general condition usually described as shock, and with pronounced nausea, vomiting, and obstipation. These findings taken in conjunction with the absence of any previous gastro-intestinal syndrome which would lead one to suspect perforating gastric or duodenal ulcer, rupture of the gall-bladder, or fulminating appendicitis, should lead one into a correct diagnosis. The condition which probably most nearly simulates superior mesenteric thrombosis is the fulminating hemorrhagic pancreatitis, but here we do not have the generalized pain, the extreme shock, obstipation, and, above all, the more or less localizing of the pain in the right abdomen.





## PERFORATING GASTRIC ULCER

THE third case is not an uncommon condition, but it presents a very uncommon syndrome and one that is not at all characteristic. The patient, a married lady, fifty-four years of age, states that, beginning about two years ago, she experienced about six attacks of pain in the left hypochondrium, lumbar region, and, to some extent, the left iliac region. The pain is sudden in onset, very severe, cramping, distinctly paroxysmal, and radiates to the left hip and to the pelvis. As a rule the pain is of such severity that it requires morphin for relief, the relief only coming after several hours. There are no associated symptoms, as nausea, vomiting, dysuria, polyuria, or hematuria. In so far as the patient knows, there was no fever either during or following the attack of pain. The attacks occurred at irregular intervals and apparently with no relation to the taking of food or drink, or to the movement of the bowels. Between the attacks the digestion was undisturbed except for a rather frequent and severe headache which, as a rule, was present about two hours after a heavy meal. The average weight was 112 pounds and the present 90 pounds, the 22 pounds having been lost gradually during the past two years.

A general physical examination of the patient failed to disclose any physical findings unusual in a woman of this age. The abdomen presented no points of tenderness, muscular rigidities, enlarged veins, tumor masses, or free fluid. The kidneys were not enlarged and the liver and spleen were not palpable. One of my assistants considered the clinical history so typical of renal colic that he ordered roentgenograms of the kidneys taken. These plates were free from shadows, which could be construed as the result of calculi in either the kidneys or the ureters. The examination of the urine and blood likewise disclosed nothing abnormal except a mild, secondary anemia. The history given by the patient most assuredly simulates that

of a renal colic more than anything else except the abdominal or renal crises of tabes, but since the neurologic investigation proved the reflexes well within the range of normal limits and the absence of any abnormal reflexes, pupillary changes, or sensory disturbances, tabes was definitely excluded. In a similar manner recurring attacks of spondylitis, diaphragmatic pleurisy, and perisplenitis were considered and excluded. Since I was able within the past few years to observe several cases of subacute perforating gastric ulcer with similar symptom complexes, a tentative diagnosis of this condition was made. A roentgenographic and roentgenoscopic examination of the gastro-intestinal tract was undertaken and the following were my deductions at that time:

**Fluoroscopic Examination of the Stomach.**—About one-third of the five-hour barium meal remains in the stomach, the remainder being in the ileum and cecum. Upon refilling the stomach it is found that the lower border lies 2 inches below the crest of the ilium. The stomach is typically of the hour-glass type. Opposite the hour-glass contraction there is, on the lesser curvature, at about its middle, a niche having all the appearances of a perforation. Above the niche there is a distinct filling defect of small size. The lower segment of the stomach is freely movable, while the upper segment, lying under the costal arch, is immovable. The duodenum is visualized well throughout, the cap being large and regular.

Several roentgenographic plates were made and the study of them did not change in the least the interpretation of the findings under the fluoroscope. The Roentgen examination of the remainder of the gastro-intestinal tract disclosed nothing abnormal.

A study of the feces, while the patient was on a blood-free diet, showed them to contain occult blood continuously. A study of the gastric contents was not attempted because of the fear of injuring the stomach during the intubation.

With the findings just delineated, a diagnosis of subacute perforating gastric ulcer with hour-glass contraction was made. The patient was placed in bed and given 4 quarts of milk daily.

She was also given some sodium bicarbonate, bismuth subcarbonate, and magnesium oxid. She seemed to feel well and was free from pain during this time. After three weeks had



Fig. 275.—Picture revealing the hour-glass contraction, the perforating ulcer at A, and, immediately above, the filling defect.

elapsed a second x-ray plate was made of the stomach and I know you can discern a marked change at the site of the perforation, although the hour-glass contraction remains. In spite of

the apparent disappearance of the perforation under dietetic and medicinal treatment, the patient was advised to have the stomach operated. To this she readily consented and was



Fig. 276.—A plate made of the stomach three weeks after Plate I, revealing the hour-glass contraction, the filling defect, and the absence of the shadow of perforation.

referred to the surgical services of Dr. McKay who, at operation, found an ulcer about midway of the lesser curvature, perforating into the substance of the pancreas. The contiguous

portion of the pancreas was pronouncedly infiltrated by an inflammatory process. The filling defect disclosed in the Roentgen examination resulted from pressure of an enlarged portion

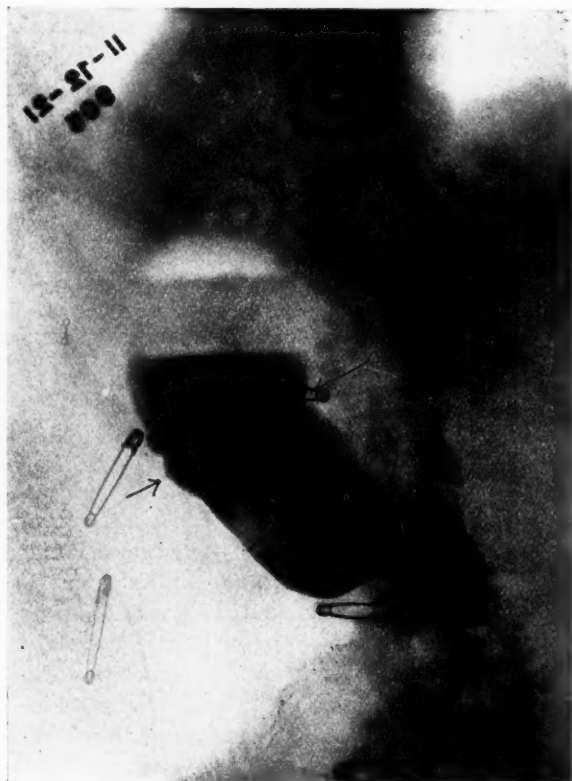


Fig. 277.—x-Ray plate of the stomach as the patient left the hospital, revealing a very small stomach with the line of suture at arrow.

of the pancreas into the gastric wall. There were dense adhesions uniting the stomach and the pancreas over a rather large area around the perforating ulcer. The hour-glass contraction was found to result from fibrous bands which almost encircled the stomach and were surely inflammatory in origin.

Our surgeon at once decided upon a midgastric resection and removed about the middle third of the stomach. Following the operation the patient, in the surgical vernacular, made an uneventful recovery and at present weighs 124 pounds.

I have here the x-ray plates made of the stomach the day before she left the hospital, which was three weeks after the operation. For some time it was necessary for her to eat six meals each day because of the small size of the remaining stomach. At the present time, however, she eats only four.

## CLINIC OF DR. DREW LUTEN

BARNES HOSPITAL

### ON THE USE OF DIGITALIS IN THE TREATMENT OF PATIENTS WITH DIFFERENT TYPES OF HEART DISEASE

DIGITALIS is one of the most widely used of drugs. It is employed in the treatment of vastly different types of heart disease, sometimes with remarkable benefit, sometimes with results that are equivocal, and sometimes with effects that are positively harmful to the patient. This uncertainty in the employment of digitalis must be attributed to two facts: First, cardiac patients too frequently are not differentiated with sufficient exactness. Improvement in one case, therefore, may lead the physician to expect an equal improvement in another patient whose symptoms may be somewhat similar, but whose cardiac involvement may be of quite different type. Second, the action of the drug, and the mechanism by which its results are accomplished may often be too little understood by the clinician. He may expect improvement from digitalis under circumstances which do not warrant such expectation of benefit. Neither experimental nor clinical pharmacologists, indeed, are in entire accord regarding certain phases of digitalis action, but recent advancement has been rapid, and has now gone far enough to clear up much of the uncertainty that has heretofore existed regarding the action of the drug and the indications for its employment.

In order to illustrate the action of digitalis in certain types of cardiac patients, and to present clearly the question of its administration to others, a few patients who have recently been digitalized will be shown, the results noted, and the action of the drug briefly discussed; other patients with heart disease will

be presented who exhibit certain findings that render the advisability of digitalis administration questionable.

**Case I.**—A white man, fifty-three years of age, admitted to the hospital nine days ago. He had typhoid at twelve; influenza, of three weeks' duration, in 1918. He had had slight dyspnea for two years, but no other symptoms referable to his heart until about a week before admission to hospital, when he noticed considerable dyspnea and weakness. These symptoms increased and were present upon admission. When first examined he was somewhat cyanotic, there was considerable edema, the liver extended 7 cm. below the costal margin, there was a blowing systolic murmur at the apex, the cardiac dulness extended  $13\frac{1}{2}$  cm. to the left in the fifth intercostal space, and  $3\frac{1}{2}$  cm. to the right in the third interspace. There were frequent extrasystoles; heart regular, rate 105; the T wave of the electrocardiogram was negative in Lead I, and the Q. R. S. interval was 0.11 second. The urine showed a trace of albumin and an occasional hyaline cast. Non-protein blood nitrogen 59; blood-pressure 160/88; Wassermann negative. The diagnosis was: Myocarditis, chronic; nephritis, chronic. He belongs to the type that is usually called myocardial insufficiency.

He was kept in bed for seven days. During this time his symptoms improved a little, the pulse declined to a mean level of 80, the edema disappeared, and the liver decreased to  $4\frac{1}{2}$  cm. The urine output improved a little, and for the last four days was 1150, 1250, 1300, and 1350 c.c. respectively.

He was then given 10 c.c. of tincture of digitalis in ten hours. His estimated dosage of this tincture (making no allowance for "non-visible" edema) would have been 19.7 c.c. He had, however, been taking undetermined amounts of the drug just prior to admission, and it was thought unsafe to administer a dose larger than the one chosen. He received the first dose of digitalis forty-eight hours ago. Now he feels considerably better. There has been no nausea. His dyspnea is improved, although he is still somewhat dyspneic. The most striking effect of digitalis has been a diuresis accompanied by a sharp decrease



in the size of the liver and a loss of weight. The day before digitalis administration his weight was 160 pounds. Today it is 141 pounds. We may expect still further weight reduction and liver shrinkage along with large urine output. His pulse-rate during these two days has varied between 72 and 90, mean 78. It is evident, therefore, that whatever the mechanism by which digitalis produced improvement in this patient, the beneficial effect was not dependent upon a change in heart rate. This matter will later receive brief discussion.

**Case II.**—A negro man, forty-eight years of age, admitted to hospital ten days ago. He had sore throat a few times about twenty years ago, gonococcus infection ten years ago, and a primary sore twelve years ago. For the past three or four months he had noticed some weakness and cough. During the last month of that time he became dyspneic and somewhat edematous.

When admitted the following findings were noted: Orthopnea; moderate edema; liver 10 cm. below costal margin; heart, dulness 14.5 cm. to the left, 2.5 cm. to the right, soft systolic murmur at apex and over precordium; urine 1.5 gm. albumin; hyaline and granular casts; blood-pressure 196/112. The electrocardiogram showed the T wave negative in Lead I, Q. R. S. interval 0.1 second; Wassermann 4+.

During seven days' observation his dyspnea did not improve. Cheyne-Stokes' respiration developed. He required morphin every night because of cough and dyspnea. His weight remained practically constant, the edema persisted, the urine output averaged about 500 c.c., and his pulse-rate remained at an approximate level of 90 per minute. There had been a slight decrease in the extent of the liver (about  $1\frac{1}{4}$  cm.). The blood-pressure varied very little. This patient, then, presented a picture much the same as the case just shown. He was suffering from myocardial insufficiency. There were, however, these differences: He showed less evidence of improvement from rest, his heart rate remained at a higher level, and there was the probable etiology of early luetic myocarditis.

He was given 10 c.c. of tincture of digitalis at 8 P. M. His weight was 186 pounds. It had been intended to administer 6 c.c. more in divided doses on the day following, but the results of the initial dose were so striking that the remainder was omitted. That night he slept without morphin, his urine output was 2500 c.c., and his weight next morning was 11 pounds less than on the preceding morning. By the next day his weight had fallen another 11 pounds and he was free of cough and dyspnea. The urine output for the twenty-four hours following the administration of digitalis was 5200 c.c. This morning, sixty-two hours after receiving the drug, he looks and feels quite comfortable, there is no edema, and the liver cannot be felt. His weight is 160 pounds. His blood-pressure, which remained high for two days, has fallen to 155/100, and his pulse, which showed little change in rate for the first two days, is now 70 per minute.

While this patient's pulse is slower than it was before the administration of digitalis, there is little evidence that the slowing was a factor in the improvement. Indeed, it seems to have been a result, rather than the cause, of the improved circulation. The diuresis began within a few hours after digitalis administration, while the heart rate at that time was unchanged. After the improvement of the circulation—which was evidenced by prompt diuresis, shrinkage of the liver, loss of edema, and relief of symptoms—the heart rate declined from the abnormally high level that it had maintained, and reached a normal rate. The first patient, however, *whose rate had not been high*, showed the same signs of improvement from digitalis, *without reduction of heart rate*. Such observations, many times repeated, convince us that in an adult whose cardiac mechanism is normal, sinus slowing is not to be expected as a direct result of the use of digitalis in therapeutic doses. If the rate of such patients is high to begin with, it usually becomes lower *after* the improvement of the circulation that follows digitalis administration; if the rate is not high to begin with, there is usually no slowing. After the administration of amounts of the drug so large that toxic rhythms are induced and the cardiac mechanism

otherwise disturbed, we have observed sinus slowing of considerable extent. But this is a toxic effect. *Sinus slowing should not be one of the objects of digitalis therapy.* This point will be referred to again.

That slowing of a rapidly contracting ventricle, however, is desirable in patients with heart failure cannot, of course, be questioned. And in certain abnormal cardiac mechanisms this can be accomplished directly by therapeutic doses of digitalis, but not when the mechanism is normal. When the auricles are in a state of fibrillation, and the ventricles are contracting irregularly and at rapid rate, the rate of the ventricles can then be slowed by digitalis. Such a result was accomplished in the next patient.

**Case III.**—A white man, age forty, admitted to hospital eight days ago. He was in this hospital four years ago and again three years ago, at which times the diagnosis was cardiac decompensation; mitral stenosis; auricular fibrillation. When examined, upon his present admission, he had considerable edema, liver just palpable, dulness at the base of the right side of chest. The heart rhythm was absolutely irregular, and there was a considerable pulse deficit; apex rate 144, pulse-rate 100. There was a snapping first sound at the apex and a systolic murmur. Later there appeared the characteristic diastolic rumble. There was moderate enlargement of the cardiac outline. His weight was 152 pounds.

For three days he received no cardiac medication. During this time he improved somewhat, but was still quite dyspneic. On the third day his weight was 151½ pounds, heart rate 135, pulse 100. At that time he was given tincture of digitalis as follows: at 10 A. M., 10 c.c.; at 6 P. M., 5 c.c.; at 9 A. M. next day, 2½ c.c.; and at noon, 2½ c.c. He improved rapidly following the administration of digitalis in spite of nausea, which was of considerable extent on the day following the administration. The dyspnea and feeling of weakness disappeared within a few days, the urine output was increased, and his weight decreased. To-day he looks and feels quite comfortable; his weight is 138 pounds.

It will be observed that the effects of digitalis in this patient have been identical in character with the results obtained in the two patients just seen. All three were improved symptomatically and freed of edema. In all three the efficiency of the circulation increased. It was noted that this increased efficiency of the circulation occurred without a lowering of ventricular rate in the first patient, and preceded ventricular slowing (which was of slight extent) in the second patient. It must, therefore, have been independent of any change in ventricular rate in those patients, and must have been produced in some other way than by slowing the ventricle.

This patient with auricular fibrillation, however, showed, in addition to the results that were noted in the other patients, a *coincident* ventricular slowing. His ventricular rates, as recorded by the electrocardiogram, were as follows: On the day before digitalis was started, 144; two hours after the last dose, 84; on the morning of the succeeding day, 36; twenty-four hours later, 48. This extensive slowing was due to the well-known action of the drug in depressing the conductivity of the a-v bundle, and thus protecting the ventricle from many of the stimuli that had previously been able to reach it. In other words, the slowing resulted from a measure of heart-block.

That such slowing was beneficial cannot be questioned. But to assume that it was the only factor in the improvement of this patient is unreasonable. In the two patients whose cardiac mechanism is normal, depression of a-v conduction caused no ventricular slowing. Some other action of digitalis, therefore, must have been in operation in those two patients to produce the beneficial results. And if in them, why not also in the third? The patient with auricular fibrillation certainly was subject to the same action of the drug that caused prompt improvement in the two other patients.

There is strong evidence, both experimental and clinical,<sup>1</sup> that this action of the drug by virtue of which the circulation is

<sup>1</sup> Luten, Drew: Clinical Studies of Digitalis; I. Effects Produced by the Administration of Massive Dosage to Patients with Normal Mechanism, Arch. Int. Med. To be published.

improved is some sort of direct action upon the musculature of the ventricle. In addition to this direct action upon the ventricle, the patient with auricular fibrillation received further benefit through the ventricular slowing. His ventricle was allowed more rest. Had his cardiac mechanism been normal, however, and the ventricle beating at a rate of 144 per minute, we could not have expected slowing except as a possible indirect effect such as would follow improvement from any cause. The point of the matter is this: Myocardial insufficiency is an indication for digitalis; auricular fibrillation, with rapid ventricular rate is an indication for digitalis; tachycardia *per se* is not an indication for the drug. *Tachycardia may even constitute a distinct contraindication*; whether it does or not depending upon the cardiac mechanism involved in the tachycardia.

It has been shown experimentally<sup>1</sup> that when the heart is poisoned by digitalis the administration of further amounts of the drug eventually produces auriculoventricular dissociation and tachycardia both of auricle and ventricle. Some of our patients who received large amounts of digitalis showed these phenomena.<sup>2</sup> The patients whose symptoms were indicative of the more severe intoxication from the drug showed ventricular tachycardia of various types. Such manifestations of the action of large doses of digitalis have only recently been recognized in patients. Certain older records of our heart station, studied in conjunction with their accompanying clinical histories, clearly indicate that patients who have developed tachycardia as a result of digitalis administration have, upon occasion, received further amounts of the drug. Serious consequences may follow and have followed such a procedure.

When a patient, therefore, who is receiving digitalis develops a tachycardia, the question must at once arise whether the tachycardia may not itself be the result of digitalis ad-

<sup>1</sup> Robinson and Wilson: A Quantitative Study of the Effect of Digitalis on the Heart of the Cat, Jour. Pharm. and Exp. Therapeutics, x, 491, January, 1918.

<sup>2</sup> Luten, Drew: Clinical Studies of Digitalis; II. Toxic Rhythms. To be published.

ministration and thus be an expression of the toxic action of the drug. Such a question is presented in the next patient.

**Case IV.**—This patient, a man aged forty-seven, was admitted to this hospital two months ago. At that time the diagnosis was myocardial insufficiency. The cardiac mechanism was normal. His liver was much enlarged. The patient was digitalized rapidly and the liver quickly receded beneath the costal margin. He continued to improve and left the hospital after a stay of two weeks.

While at home he took from 10 to 20 drops of tincture of digitalis three or four times a day during most of the time for six weeks. His improvement was gradual, but rather progressive until two nights ago. At that time he noticed that his heart was "jumping" and that he had pain in the cardiac region. His pulse yesterday was 164, regular. Previous to that time the pulse-rate had been usually 70 or 80. His digitalis was stopped and he was advised to enter the hospital. Today he has rather an ashen appearance. There is no edema. The liver extends about 9 cm. below the costal margin. He is somewhat dyspneic. The apex rate is 164, rhythmic. Neither vagus pressure nor mild exercise affects the heart rate. He comes to the hospital for more complete examination, which should include the taking of electrocardiograms.

Should this patient receive digitalis? The answer to this question must await the result of further study. He again shows to some extent the same evidences of myocardial insufficiency which were present upon his former admission and which yielded promptly to digitalis. It is possible that the tachycardia is the result of auricular flutter with 2 : 1 block. If these were the only considerations to be disposed of, he should unquestionably receive large doses of digitalis. But the problem presents another, and a very important aspect. It may be that the amounts of the drug which he has been taking have been sufficient to produce the tachycardia. For all we know the patient may have a toxic rhythm *due to digitalis*—possibly an idioventricular rhythm. If such should be the case, the adminis-

tration of further amounts of the toxic agent might easily be enough to produce ventricular fibrillation<sup>1</sup>—a result which Robinson and Wilson found to occur after the administration to animals of very little more of the drug than the amount sufficient to produce idioventricular tachycardia.

At this moment we know neither the cause nor the point of origin of this patient's tachycardia. If it is of sinus origin it constitutes no indication for digitalis—it might even then be a result of the digitalis he has had. If it is of ectopic origin it is difficult to see how digitalis would stop it. It would appear, indeed, that the abnormal mechanism in such a case would be more likely to be accentuated by the drug even though the digitalis that he has had were not the exciting factor in its production. If, on the other hand, the tachycardia is that of 2:1 flutter, the patient should receive digitalis. In such a mechanism the drug usually produces ventricular slowing by depression of a-v conduction, whether or not it brings about fibrillation of the auricles. But the patient is not severely decompensated and there is, therefore, no urgent indication for digitalis. His chief symptom is tachycardia. That, in itself, is not an indication for the drug, but since it may even be due to excessive amounts of digitalis already administered, the giving of additional doses at this time might result fatally.

**Case V.**—This patient, a woman twenty-three years of age, was admitted two days ago. She was told by her doctor a year or more ago that she had heart trouble, but she had no cardiac symptoms until three months ago. Following a forceps delivery at that time she began to notice dyspnea, cough, swelling of abdomen, and palpitation. Her condition upon admission was much the same as it is today. You notice the marked dyspnea, cyanosis, and edema. The liver extends about 9 cm. below the costal margin. There is a vigorous cardiac pulsation as far as the anterior axillary line. There is a thrill at the apex, hard to time, but which appears to be diastolic; also a short diastolic and a loud systolic murmur. The heart action is regular, rate

<sup>1</sup> Robinson and Wilson: *Loc. cit.*

124. The vital capacity is 450 c.c. The blood-pressure is 165/100. The urine contains a large amount of albumin and many casts. Wassermann negative.

The heart is in a state of extreme decompensation. The diagnosis is cardiac hypertrophy and dilatation; mitral disease (stenosis and insufficiency). If our knowledge of her case went no farther, we should decide that she should receive digitalis immediately. But there is another very important consideration. On admission her heart rate was 100, pulse-rate 55. Auscultation revealed a persistent bigeminy. The electrocardiogram showed that this bigeminy was due to a constant coupling with long pauses between the couplets. The first beat of the couplets is of the same type that is shown in the electrocardiogram taken a few hours ago in which the mechanism is normal. The second complex of the couplets that were present on admission was an ectopic ventricular complex. The electrocardiogram further showed auricular fibrillation. The ventricular responses to auricular impulses were irregular. Their rate, however, was only 55. In other words, there was a high degree of a-v block. The coupling was also further evidence of the action of some toxic agent.

Now, the commonest toxin which produces these phenomena is digitalis. Although the patient had not been under the care of a doctor for a month, she had been taking a "patent heart medicine." The electrocardiogram of yesterday still showed auricular fibrillation and the coupling. Today, however, the mechanism is normal, rate 124. Whether or not this patient has had some drug of the digitalis group in toxic amounts we do not know. But we do know that her heart gave evidence of having been affected by some poison which acts like digitalis, and that after two days without the patent medicine these toxic signs are less in evidence. In spite of the evident cardiac insufficiency and the auricular fibrillation, therefore, she was not given digitalis. And since the toxic agent cannot be regarded as having been entirely eliminated as yet, she should not receive digitalis at this time.

In considering the question of administering digitalis to



the last two patients, the danger of eliciting further toxic effects from its use clearly constituted a contraindication which outweighs the indications for its employment. In other cases, in which toxins of a different nature have affected the heart to a greater or less extent, a decision may not so readily be reached. Such a problem is presented by the next patient.

**Case VI.**—This patient, a boy of fifteen, was in good health until about six weeks ago. At that time he had a sore throat for a few days. About ten days later he began to have fever and to be somewhat drowsy. After a few days of this he had pains in his knees and ankles for two or three days. Since then he has had considerable fever and has been quite weak. When first examined seven days ago his chief complaints were dyspnea and pressure in the chest. His temperature was  $101^{\circ}$  F., pulse 132. There was no evidence of arthritis; no edema. There was a wide area of pulsation over the precordium; dulness 14 cm. to the left in the fifth intercostal space and  $5\frac{1}{2}$  cm. to the right in the fourth. There was a systolic murmur at the mitral area, a diastolic murmur at the aortic, and a pericardial friction in the left second and third interspaces. The electrocardiogram showed the signs of right ventricular preponderance and a P-R interval of 0.19 second. Pericardial puncture gave negative result. The diagnosis was: Rheumatic fever, cardiac dilatation, acute fibrinous pericarditis, acute myocarditis.

During the next two days the pulse-rate showed a slightly downward tendency, the recorded extremes being 110 and 120. There was some discussion as to the advisability of digitalis administration. The drug was ordered after two days, 10 minims of the tincture four times a day. This was continued for three and a half days, during which time he received 140 minims. It was discontinued two days ago because of nausea and vomiting. There was no appreciable effect upon the pulse-rate. Yesterday the extremes were 108 and 120, today the rate is 115. The electrocardiogram, however, showed a lengthened a-v conduction time—the usual result of digitalis in such cases—the P-R time yesterday being 0.30 second.

Has this patient been benefited by digitalis? He received an amount of the drug sufficient to produce nausea and vomiting and to produce characteristic changes in the electrocardiogram. Symptomatically he is somewhat better than he was upon admission, but the improvement had been progressive and gradual, and the rate of improvement has not been increased since the drug was given. There has been no lowering of pulse-rate in spite of the evident action of the drug upon the heart. There is no evidence that the administration of digitalis was beneficial to the patient.

The argument advanced in favor of giving the drug to this patient was that by its action upon the ventricular musculature, by virtue of which systole is improved, it would tend to overcome the cardiac dilatation. It is difficult to see how the action of the drug could effect such a result. In the first place, we neither surely know nor fully understand the exact mechanism by which it improves the circulation by its action upon the muscle of the ventricle. But, assuming that this result is effected by a strengthening of contraction in some way, such an effect is exactly what we wish to avoid in acute inflammation of the heart muscle. Our therapy is directed toward resting the heart, not toward working it. All signs in this patient indicate not so much a failure of the circulation as a toxemia of the heart. That such failure would ultimately ensue if the action of the toxic agent is continued long enough cannot be denied, but at this time it is not the object of our therapy. That object is the overcoming of the effect of some toxic agent upon the heart. Why, then, subject the heart to the further action of a toxic drug? If digitalis would decrease the rate of such a heart, such an action of the drug would constitute an important indication for its administration. But it did not lower the rate. Instead of this *it gave (electrocardiographic) evidence of increased toxic effect.*

It may well be questioned whether the effects of digitalis in patients with acute myocarditis may not be positively harmful. Its action in such cases may be literally to add insult to injury. In the absence, therefore, of any definite indication for its

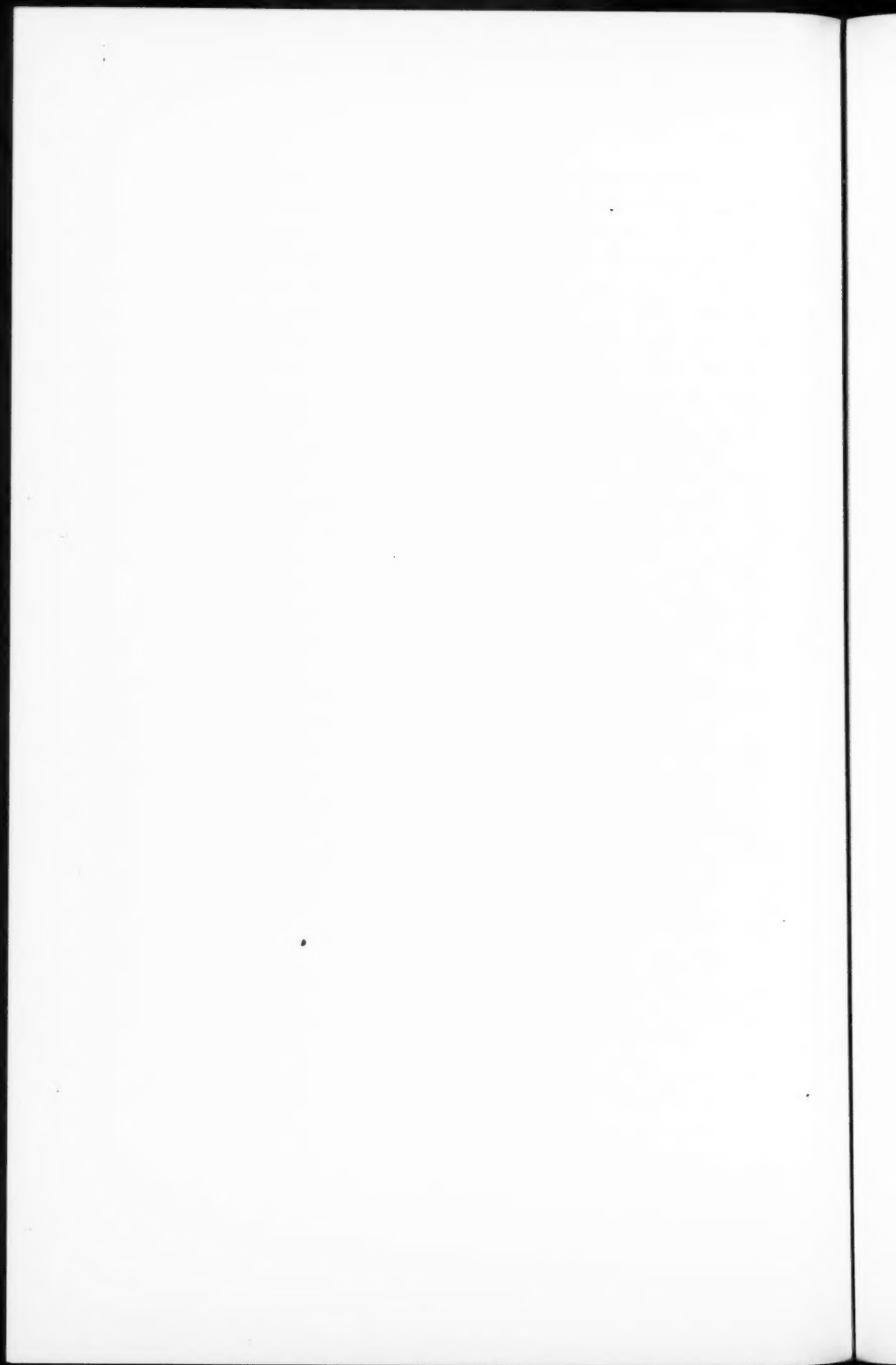
employment in such cases it would seem, at present, that it should not be administered. The question must receive further study.

**Summary.**—Two patients with myocardial insufficiency and normal mechanism, one with pulse-rate somewhat increased, and one with normal rate, were digitalized. Both were improved. Slowing was not a factor in the improvement. One patient with myocardial insufficiency and auricular fibrillation who was digitalized also improved. Marked ventricular slowing accompanied the improvement.

A patient who had been taking digitalis developed tachycardia. In spite of certain indications for the drug, digitalis was stopped in view of the fact that tachycardia is one of the toxic effects of digitalis. The great danger from further dosage, in such a contingency, was emphasized.

A patient with auricular fibrillation, whose findings indicated both myocardial insufficiency and the action of some toxin like digitalis, was shown. Digitalis was withheld.

A patient with acute rheumatic myocarditis and cardiac dilatation received relatively small amounts of digitalis. There was no improvement from the drug, but the electrocardiogram showed a marked lengthening of the P-R interval. The advisability of administering digitalis to such a patient, unless other more unequivocal indications for its use are present at the same time, was questioned.



## CLINIC OF DR. HORACE W. SOPER

ST. LUKE'S HOSPITAL

### BENIGN PYLORIC OBSTRUCTION IN THE AGED

INASMUCH as benign obstruction of the pylorus may occur at any period in life we must define what we mean by "aged." The young person of sixty or seventy may object to the term, but we will compromise and consider sixty-five years as marking the onset of advanced age.

The subject is of importance for the reason that lesions of the pylorus sufficient to produce stenosis are malignant in nature in the large majority of the cases. When occurring late in life the benign cases are, therefore, more apt to be diagnosed as cancerous, and operative procedure not advised because of the age and debility of the patient. No doubt many such patients are permitted to die with the diagnosis of cancer, inasmuch as the symptomatology would readily lead one to commit the error. A patient of advanced years presenting a palpable epigastric mass, with pain, nausea, vomiting, loss of weight, and strength is usually dismissed as having advanced cancer and, therefore, beyond the reach of surgical aid. The differential diagnosis between benign and malignant obstruction of the pylorus presents considerable difficulty. In fact, differentiation may be impossible in some cases. Even at operation the surgeon may experience difficulty in determining the nature of the growth, particularly as the dictum has gone forth that no piece of the mass may be excised for microscopic examination.

The pathology of benign stenosis occurring in the aged is, as a rule, limited to the cicatricial contractures and hyperplasia produced by gastric and duodenal ulcer. Chronic hyperplastic stenosis secondary to chronic gastritis is rarely found after the age of sixty-five. The benign new growths, such as myoma, lipoma, and lymphadenoma, are rare at all ages, and extremely

rare in advanced age. The diagnosis of pyloric stenosis at this time of life, therefore, resolves itself into a differentiation between obstructive ulcer and cancer. The old rule that in cancer Oppler-Boas bacilli and lactic acid are found in the stomach contents still holds good in cases where free HCl is absent. However, in many cases of cancer free HCl is present. In obstructive ulcer the HCl content is apt to be high and sarcinae present if stasis is prolonged. Occult blood determination in the feces by means of the guaiac test is of importance. A strong persistent reaction means cancer. The cicatricial ulcer in the aged rarely bleeds. However, we must remember that cancer may progress to fatal conclusion without showing occult blood reaction. The clinical history is by far the most important element in differentiating between the two conditions. In the benign cases an "ulcer history" is obtainable, usually extending over a long period of years. In carcinoma the onset of the disease is more definitely marked and is of shorter duration. As a rule the patient has not had previous stomach disorders. The confirmed dyspeptic rarely winds up his career as a cancer victim. The Roentgen-ray findings may be of aid in distinguishing irregularities in cancerous growths. However, merely gastric retention due to pyloric stenosis is the usual x-ray diagnosis.

The development of cancer on an ulcer basis does not happen as often as formerly contended. Clement R. Jones<sup>1</sup> has recently shown that it is an extremely rare occurrence. There was no such transition in any of our series of cases. Reports of 9 cases follow. The histories are abstracted so that only the salient points directly bearing on the case are mentioned. In nearly all of them complete x-ray of the gastro-intestinal tract, blood examination, urinalysis, as well as physical examination, was made. When the above tests were not made special mention will be made in the case abstract.

#### GROUP I

**Case I.**—February, 1909. Male, aged seventy. Ulcer history extending over a period of ten years. A palpable mass size

<sup>1</sup> Read before the American Gastro-enterological Association, Boston, Mass., April, 1923.

of an orange, showing no respiratory excursion, was located in upper epigastrium. Feces negative for occult blood. Thirty pounds weight loss. Had lived on thin gruels for past year. Operation, posterior gastro-enterostomy, by Dr. Willard Bartlett. Ether anesthesia. Mass was clearly inflammatory, no glandular involvement. Profound shock symptoms followed immediately. On the second postoperative day the stomach suddenly became immensely dilated. Under local anesthesia an anterior gastro-enterostomy was done by means of the Murphy button. Recovery was slow, but finally, after many relapses, he had very good gastric function. He was alive and well at last accounts in 1915, six years after the operation.

**Case II.**—November, 1912. Female, aged eighty. Ulcer history of five years' duration. Dyspeptic nearly all her life. Patient was much emaciated and extremely weak, confined to bed, vomiting constantly, no blood. Vomitus was strongly acid and contained sarcinæ. Feces negative for occult blood. No palpable mass. x-Ray examination not made. Operation, posterior gastro-enterostomy, by Dr. H. G. Mudd. Ether anesthesia. Cicatricial mass size of lemon was found at pylorus. No glandular involvement. Exitus twenty hours later from shock.

**Case III.**—Male, aged seventy-four. Came under observation in January, 1914. Gave a typical ulcer history extending over a period of twenty-eight years. x-Ray examination showed marked gastric motor insufficiency due in all probability to duodenal ulcer. No palpable mass. Feces were negative for occult blood. Stomach contents did not show the presence of blood or sarcina. Free HCl 86, total acidity 98. He responded fairly well to dietetic treatment for four years. Finally obstruction became almost complete. Operation, posterior gastro-enterostomy, January, 1918, by Dr. H. G. Mudd. Ether anesthesia. A mass as large as an unshelled walnut was found at the pylorus. No glandular enlargement. Died of embolism fourteen hours after operation.

**Case IV.**—February, 1918. Female, aged sixty-seven. Gave a typical ulcer history with vomiting of blood. Five years' duration. *x*-Ray examination showed a gastric motor insufficiency due to duodenal ulcer. No palpable mass. She responded quite well to dietetic treatment until September, 1919, when she had almost complete obstruction and was operated on by Dr. James L. More, of Pulaski, New York, who did a posterior gastro-enterostomy under ether anesthesia. She made a good recovery and has remained well since.

**Case V.**—February, 1918. Male, aged sixty-five. Gave an ulcer history of twelve years' duration. No hemorrhages. *x*-Ray of the gastro-intestinal tract showed a gastric motor insufficiency with prolonged retention of the bismuth meal. No palpable mass. Operation, posterior gastro-enterostomy, March, 1918, by Dr. H. G. Mudd, disclosed a mass at the pylorus evidently a simple benign obstruction. Ether anesthesia. He suffered from severe shock and had stormy convalescence. Was in good condition when last heard of in 1921, three years after the operation.

## GROUP II

**Case I.**—October, 1912. Female aged seventy-one. Gave an ulcer history of twenty-five years' duration. For the past fifteen years has lavaged her stomach daily and has had considerable relief, although it was necessary to adhere to a diet of liquid foods. Dietetic treatment and lavage was continued until December, 1914, when the obstruction became almost complete. *x*-Ray examination at that time suggested the possibility of the ulcer being duodenal in character. Stomach contents showed free HCl 40, total acidity 50, no sarcinae. Feces were negative for occult blood. No palpable mass. Operation, posterior gastro-enterostomy, December 14, 1914, by Dr. Fred Murphy, disclosed the pylorus contracted down to a mass of hard firm scar tissue. Impossible to say whether ulcer sprang from the duodenal or pyloric side. Walls of the stomach were much hypertrophied. "Felt like shoe leather." Combined gas and local anesthesia. She had no shock, but vomited for five days. She



finally made a good recovery. She has eaten freely of all kinds of food and is at present in excellent health, aged eighty-two.

**Case II.**—October, 1915. Male, aged seventy-five. He gave an ulcer history of five years' duration. Hemorrhages occurred



Fig. 278.—Group II. Case II. Illustrates tremendous dilatation of the stomach before operation.

one year ago. During the past year has taken only liquid food and is exceedingly emaciated and weak. Feces negative for occult blood. Stomach contents showed free HCl 26, total

acidity 40, no sarcinae, no blood. Mass size of an orange was palpated in the epigastrium. *x*-Ray diagnosis was high-grade pyloric stenosis probably due to ulcer.

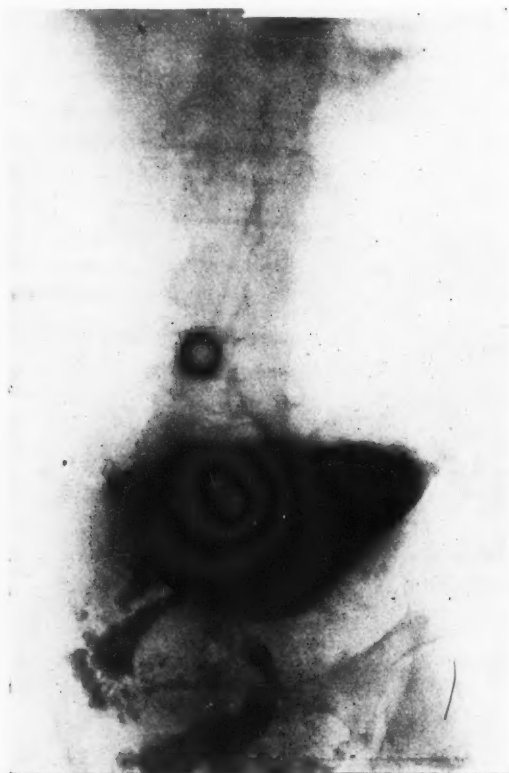


Fig. 279.—Group II. Case II. Large six-hour residue. The stomach did not clear in twenty-four hours' time.

Operation, November 4, 1915, Dr. Willard Bartlett. Because of the patient's extreme weakness anterior gastro-enterostomy was done by means of a Murphy button. A large mass was found surrounding the pylorus and causing almost complete obstruction. Several glands were enlarged along the

lesser curvature. One of them was removed and examined by the pathologist, Dr. Rudolph Buhman, who reported as follows:

Sections from tissue show a thickening of the capsule, an increase in the connective-tissue trabeculae, and many endothelial cells. Diagnosis: Inflammatory.



Fig. 280.—Group II. Case II. Same case as Fig. 278 taken one year after the operation. Note the increased tonus and the rapid filling of the small intestine through the gastro-enterostomy stoma.

He made a very good operative recovery. We have seen him on an average of once a year since the operation.

A point of great interest in this case is the fact that the

Murphy button still remains in the gastro-enterostomy stoma with admirable function. None of the bismuth meal passes through the old pyloric opening. The palpable mass disappeared entirely in one year's time. He has had trouble off and on from injudicious eating. It appears that vegetable fibers and masses of raw apples, pickles, etc., at times block the Murphy



Fig. 281.—Group II. Case II. The Murphy button has remained in the gastro-enterostomy stoma for a period of eight years.

button stoma, otherwise he has remained in perfect health. Now aged eighty-three (Figs. 278-281).<sup>1</sup>

**Case III.**—December, 1918. Male, aged seventy-five. Gave an ulcer history of twenty years' duration. Was under the care

<sup>1</sup>I am indebted to Dr. R. Walter Mills for the x-ray films.

of Dr. Jesse Meyer nine years ago, who made a diagnosis of obstructive ulcer and taught him to use the stomach-tube. Since that time he has used the tube daily, washing out a large amount of food at bedtime. Stomach contents showed HCl 19, total acidity 36. Many sarcinae and pieces of food residue eaten the previous day. Feces negative for occult blood. x-Ray examination disclosed a very marked motor insufficiency. Diagnosis was that the lesion in all probability was prepyloric in character.

Operation, posterior gastro-enterostomy, under local anesthesia (novocain), by Dr. M. B. Clopton, March, 1921. The pylorus was found embedded in a mass of adhesions attached to the lower surface of the liver. They were not disturbed. No symptoms of shock followed the operation. Patient made a rapid recovery and has remained in perfect health. Now aged eighty. This patient after so many years of dietetic restrictions literally "eats everything."

**Case IV.**—November, 1921. Male, aged sixty-eight. Gave an ulcer history of two years' duration. No hemorrhages. Feces negative for occult blood. Because of the weakened condition of the patient no test-meal was given. Vomitus, however, showed the presence of sarcina and strong HCl reaction.

x-Ray examination revealed marked obstruction at the pylorus due to duodenal ulcer. Operation, September 20, 1922, posterior gastro-enterostomy, by Dr. Willard Bartlett under local anesthesia (novocain). Stomach found dilated with thickened walls. There were dense adhesions between the pyloric region and the abdominal wall just under the liver. The pylorus was a hard mass size of a lemon consisting of dense fibrous connective tissue. No glandular enlargements. No shock symptoms ensued, no nausea, no vomiting. He made a good recovery and is in good health at the present time.

#### CONCLUSIONS

All of the above cases were poor operative risks. The 5 cases cited in Group I were operated upon with ether as the anesthetic.

The two deaths might possibly have been avoided by employing local anesthesia. However, the risk under a general anesthetic is certainly justifiable.

Local anesthesia was used in all the cases in Group II without mortality. Rapid recovery and ability to take care of all kinds of food was truly remarkable. All these aged patients seemed determined not to submit to any dietetic restrictions whatsoever. The average gastro-enterostomy patient is carefully dieted and readily submits to dietetic regulation. One of our most important clinics years ago almost invariably closed an ulcer operative case history with the words, "He now eats everything." At the present time this same clinic never fails to give a definite diet list to all their postoperative stomach cases. The probable cause of such immunity in the aged is explained by the pathology. The dense fibrous connective-tissue hyperplasia produces a stenosis that results in a hypertrophy of the stomach walls—conditions that favor good function in the gastro-enterostomy stoma. Moreover, there is little or no chance for further ulcerative process about the pylorus.

## METABOLISM CLINIC OF DR. WILLIAM H. OLMSTED

BARNES HOSPITAL

---

### THE VALUE OF WEIGHT CURVES IN DETERMINING THE SEVERITY OF DIABETES

It has been our experience that physicians fail somewhat to evaluate the degree of severity of diabetes. Hospital observation is not necessary in determining the degree of severity. As much can be learned from taking a careful history as from laboratory observations. Diabetes is much more a clinical disease than a laboratory one. It is our purpose here to present the history with special reference to the weight curves of different classes of patients and predict, before the laboratory examinations are made, the probable severity of the case.

The value of weight curves in predicting the degree of the disease depends upon certain basic assumptions. These assumptions have been proved repeatedly and the facts are well brought out in Joslin's book:

1. It is well known that the diabetic acquiring the disease when under thirty-five years of age will, in the majority of instances, have the disease in a severe form and usually run a rapid downward course. The result of his diabetic condition is to bring the weight rapidly to a level below the normal for his height and age. This fact has been proved to be true. Suppose, however, that we find in the young diabetic a weight that is normal for his age, or even above normal, what assumption can be made? If for several months or perhaps a year sugar has been found and the weight is still normal, one may assume that the patient has only a mild degree of diabetes and is therefore an exception to the general rule, or that true diabetes does not exist. If there has been sugar in the urine without loss of weight for a period of three or more years, it is safe to assume that true diabetes is not present.

The two deaths might possibly have been avoided by employing local anesthesia. However, the risk under a general anesthetic is certainly justifiable.

Local anesthesia was used in all the cases in Group II without mortality. Rapid recovery and ability to take care of all kinds of food was truly remarkable. All these aged patients seemed determined not to submit to any dietetic restrictions whatsoever. The average gastro-enterostomy patient is carefully dieted and readily submits to dietetic regulation. One of our most important clinics years ago almost invariably closed an ulcer operative case history with the words, "He now eats everything." At the present time this same clinic never fails to give a definite diet list to all their postoperative stomach cases. The probable cause of such immunity in the aged is explained by the pathology. The dense fibrous connective-tissue hyperplasia produces a stenosis that results in a hypertrophy of the stomach walls—conditions that favor good function in the gastro-enterostomy stoma. Moreover, there is little or no chance for further ulcerative process about the pylorus.



## METABOLISM CLINIC OF DR. WILLIAM H. OLMSTED

### BARNES HOSPITAL

---

#### THE VALUE OF WEIGHT CURVES IN DETERMINING THE SEVERITY OF DIABETES

It has been our experience that physicians fail somewhat to evaluate the degree of severity of diabetes. Hospital observation is not necessary in determining the degree of severity. As much can be learned from taking a careful history as from laboratory observations. Diabetes is much more a clinical disease than a laboratory one. It is our purpose here to present the history with special reference to the weight curves of different classes of patients and predict, before the laboratory examinations are made, the probable severity of the case.

The value of weight curves in predicting the degree of the disease depends upon certain basic assumptions. These assumptions have been proved repeatedly and the facts are well brought out in Joslin's book:

1. It is well known that the diabetic acquiring the disease when under thirty-five years of age will, in the majority of instances, have the disease in a severe form and usually run a rapid downward course. The result of his diabetic condition is to bring the weight rapidly to a level below the normal for his height and age. This fact has been proved to be true. Suppose, however, that we find in the young diabetic a weight that is normal for his age, or even above normal, what assumption can be made? If for several months or perhaps a year sugar has been found and the weight is still normal, one may assume that the patient has only a mild degree of diabetes and is therefore an exception to the general rule, or that true diabetes does not exist. If there has been sugar in the urine without loss of weight for a period of three or more years, it is safe to assume that true diabetes is not present.

2. In older persons, past the age of forty, the disease is usually mild, and we find patients overweight, even after having had the disease as long as five or six years. It has been our experience that 75 per cent. of the diabetics who are over forty-five years of age are overweight. The amount of weight lost is not so significant as the weight at the onset of the disease, that is, if a patient is 30, 40, or 50 pounds above the normal weight for age and sex at the onset of the disease, the loss of this amount of weight is not nearly so significant as the loss of from 30 to 50 pounds when the weight at the onset is normal. These points may be shown in the following computations:

Man 5 feet, 7 inches (170 pounds); normal weight at fifty years, 157 pounds.

*If weight is normal, calories required:*

Basal metabolism.....	1640 calories
Work calories (approximate) ..	1000 "
Total .....	2640 "

Probable distribution of food:

Protein, 100 gm. equals.....	400 calories
Fat, 100 gm. equals.....	900 "
Carbohydrate, 325 gm. equals.....	1300 "
Total .....	2600 "

*If weight is 30 pounds above normal (187 pounds), calories required at fifty years:*

Basal metabolism.....	1750 calories
Work calories ( $\frac{187}{157} \times 1000$ ) equals.....	1190 "
Total .....	2940 "

Probable distribution of food:

Protein, 100 gm. equals.....	400 calories
Fat, 100 gm. equals.....	900 "
Carbohydrate, 410 gm. equals.....	1640 "
Total .....	2940 "

*If weight is 30 pounds below normal (127 pounds), calories required:*

Basal metabolism.....	1500 calories
Work calories ( $\frac{127}{157} \times 1000$ ) equals.....	810 "
Total .....	2310 "

Probable distribution of food:

Protein, 100 gm. equals.....	400 calories
Fat, 100 gm. equals.....	900 "
Carbohydrate, 250 gm. equals.....	1000 "
Total .....	2300 "

The assumption is made that the normal amounts of protein and fat are usually about 100 grams of each, and when calories are increased they are usually increased by increasing the carbohydrate consumption. Carbohydrate foods furnish 50 to 60 per cent. of calories, fat 25 to 35 per cent., and protein 10 to 20 per cent.

The above shows that a man 5 feet, 7 inches tall, at normal weight, requires about 2600 calories; that when he is 30 pounds above normal he requires 2900 calories, the increase in calories usually being supplied by carbohydrate. The change in work calories is assumed to be proportional to change in weight. On the other hand, if the same man be 30 pounds below the normal weight, his calorie needs will be only 2300 and the carbohydrate requirement about 250 gm. per day. Thus, when a diabetic's weight falls from 30 pounds above normal to normal and remains at about this level, he must necessarily still have a fairly good carbohydrate tolerance. Of course, the patient's diet is usually changed somewhat by the physician when sugar is discovered in his urine, and this is a factor in the rapidity of his loss in weight; I do not believe it is an important factor. On the other hand, if a man who is normal in weight at the onset of the disease loses 30 pounds, his carbohydrate tolerance will necessarily be lower, because he will not need as much carbohydrate at this gradually reduced level of metabolism. The above statements have been made assuming that the metabolism, when a patient is 30 pounds underweight, is normal. As a matter of fact, when a patient loses 30 pounds his basal metabolism, in all probability, is considerably below normal, so that this would further decrease his carbohydrate needs. If these assumptions are correct, then in the case of a diabetic past the age of fifty who is underweight, the disease will be of a more severe grade than is usual, or else there is some other factor in addition to his diabetes that causes him to lose weight. It has been our experience that older diabetics who are underweight will present in two-thirds of the instances some infectious disease. Such infections have an important part in reducing the weight of the patient and, furthermore, in reducing his carbohydrate toler-

ance. The infectious processes, as a rule, effect a reduction in carbohydrate tolerance of themselves.

In about 40 per cent. of the cases of older diabetics who are underweight there are no complications, but the disease is of so long standing that the weight has gradually fallen to below normal, or else, in exception to the general rule, the older person has a severe type of the disease.

In taking the weight history there are certain expressions that call forth most easily the data. First of all the patient can usually remember when he weighed his maximum or when he was at his "best" weight. He can tell what his "usual" weight is, that is, what his weight was prior to the onset of the diabetes. It is also important to know the rapidity of loss in weight after the onset of symptoms. The rapidity of loss after sugar has been found will give very important data regarding the rapidity of the disease. Definite gain in weight, 10 pounds or more, after the onset of the disease is important because the diabetic cannot gain weight unless the disease is mild.

The charting of the weight curve is best done as follows:

The base line is the normal weight of the patient at any age. The figures above the base line are the pounds overweight and the figures below the base line are the pounds underweight. The horizontal line at the right represents the time at which the patient came under observation. Attention is called to the fact that the base line can represent any weight, depending on the height and age of the patient. Thus, the base line in Case I is 150 pounds, that is, 150 pounds is the normal weight for a man 5 feet, 9 inches at twenty-four years of age, while the base line in Case III represents 137 pounds, which is the normal weight for a man 5 feet, 4 inches at the age of thirty-three years. Similarly, the base line in Case VII is 167 pounds, which is the normal weight for a man past sixty years who is 5 feet, 9 inches tall.

This method of charting the weight curves of patients shows at a glance the necessary facts in each case, that is, what the patient's weight has been in respect to his normal weight at any time.

**Case I.**—Medical No. 11.005, B. T., miner, age twenty-four. Height 5 feet, 9 inches; weight 129 pounds.

Admitted to the hospital July 3, 1923, complaining of thirst and pains all over body. No family history of diabetes. Smallpox five years ago; mumps two months ago.

One year ago began to feel tired with pains generally over body, greatly increased appetite, and excessive thirst. Greatly increased volume of urine; began about this time to lose weight. Loss in weight not marked until about three months before admission.

Examination: Patient is sluggish and dull. Strong odor of acetone on breath. Respirations are deep, but not enough to be classified as air hunger. Eye-grounds show definite white arteries suggesting lipemia retinalis. The arteries are much thickened for patient's age. Enlarged glands in left side of neck.

Laboratory: On admission-blood sugar was 0.281; carbon dioxide content 15 volumes per cent. Fat content 2.14 per cent. Wassermann negative.

Urine showed a large amount of sugar and strong ferric chlorid reaction.

Course: Patient received 55 units of insulin in the first twelve hours. Blood-sugar fell rapidly to 0.04 and the plasma carbonate rose to 33 volumes per cent. The patient was given fruit juice because of insulin hypoglycemia. The blood-fat fell rapidly until the third day, when it was 0.9. With 25 units of insulin per day and 800 calories patient became sugar free. The tolerance rapidly increased until he was taking 2200 calories (P-60, F-200, Ch-60) without any insulin at all. Patient was discharged with 10 units of insulin per day and 2600 calories (P-60, F-225, Ch-100).

This case was one of acute diabetes with a moderate degree of acidosis. The weight curve (Fig. 282) shows the onset probably about one and a half years before admission to hospital. The symptoms began one year before. Patient's age, his condition of acidosis, and the very rapid loss in weight shows him to be an acute diabetic, his weight curve being typical of this particular class of patient. Our experience would lead us to

predict that the present good tolerance will gradually fail with the return of severe symptoms, and it will be necessary to give larger doses of insulin to give the patient a maintenance diet.

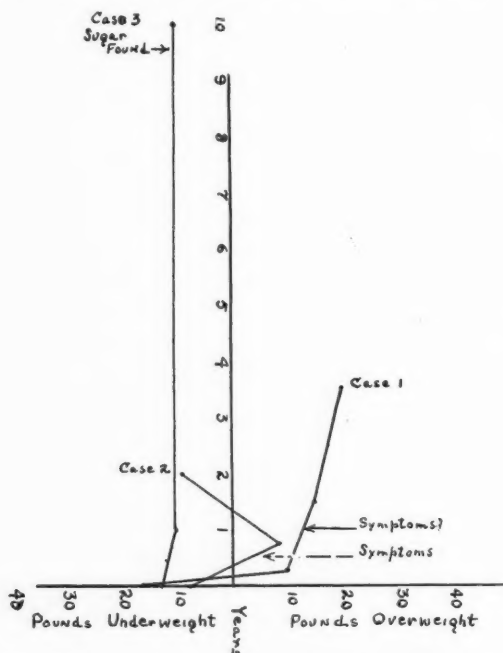


Fig. 282.—Normal weight, Case I, 150 pounds. Normal weight, Case II, 142 pounds. Normal weight, Case III, 137 pounds.

**Case II.**—Medical No. 11,150, T. P., fireman, age twenty-one, height 5 feet, 7 inches, weight 137 pounds.

Admitted July 20, 1923, complaining of sugar in urine. No history of diabetes in family; has always been in good health. A month previous his family physician noted that he looked badly and asked to examine the patient. Sugar was found in urine. Patient had been examined six months before for life insurance and had passed successfully. Patient noted that he had had excessive thirst in the spring, about three months previously,

and at the same time there was increased urination. Lost 20 pounds in the last six months.

Examination: Shows a very well-developed, muscular man, giving evidence of some loss in weight. Teeth: Many are carious, with much dental work. Tonsils are enlarged and reddened. Chest: Slight funnel breast.

Laboratory: Blood-sugar 0.17. Wassermann negative. Blood-count normal. Urine shows a few hyaline casts, no albumin. Large amount of sugar.

Course: On a diet of 1700 calories (P-50, F-150, Ch-50), patient became sugar free and the blood-sugar dropped to 0.087. He remained sugar free when raised to 2600 calories.

From the weight curve (Fig. 282) the loss of 20 pounds in weight would indicate a severer type of diabetes than later investigation showed to be present. The history of the accidental finding of sugar and the lack of symptoms such as polyuria, however, is good evidence that the disease is mild. How then explain the loss in weight? The occupation of the patient—a fireman, accustomed to daily vigorous exercise—probably explains the weight loss. This case then is an exception to the usual findings in the young diabetic in that the disease is mild, the excessive weight loss being due to vigorous exercise.

**Case III.**—M. B., Hebrew, retail jeweler, age thirty-three. Height 5 feet, 4 inches, weight 124 pounds.

Consulted a physician, complaining of sugar in urine. One brother has "sugar" in his urine. One of patient's relatives said to have diabetes. Gonorrhea three years ago. Twenty years ago had attacks in which he was semiconscious, foamed at the mouth, and became "stiff." Had these attacks for two years. Has always been very easily excited, gets discouraged easily and depressed; often feels blue. Sugar was first found ten years ago; since then it has been found by various physicians off and on. Insurance examiner found sugar, and patient was refused insurance. His diet at present consists of 10 pieces of rye bread a day, but he does not take sugar or candy.

**Examination:** Small, well-nourished man, apparently in good state of health, with no abnormalities except slightly enlarged prostate, the excretion under massage being practically pure pus.

**Laboratory:** Urine shows a trace of reducing substance on the day of examination; the following day, none. Blood-sugar 0.10. Sugar tolerance 0.8 gm. glucose per pound.

First hour blood-sugar 0.177.

Second hour blood-sugar 0.16.

Third hour blood-sugar 0.09.

**Course:** Patient has been seen at intervals for the past two years. Reducing substance has been found several times, although usually in very small amounts. The blood-sugar July, 1923, 0.087. Weight during the past two years has remained constant.

When the history that sugar had been found by a reliable physician ten years ago was obtained, it was felt that there was a great deal of doubt whether the case was true diabetes. Certainly it is very unusual that diabetes beginning at the age of twenty-three should have remained so mild for ten years (Fig. 282). A blood-sugar curve following a glucose meal and the subsequent observations of the following two years confirms the impression obtained from the history that the case is one of emotional glycosuria. Renal diabetes is ruled out because sugar has never been found constantly in the urine.

**Case IV.**—Medical No. 11,159. N. M., housewife, age forty-nine. Height 5 feet, 3 inches, weight 139 pounds.

Entered hospital complaining of sugar in the urine, July, 1923. No history of diabetes in the family; has never been ill. Ten years ago patient became excessively thirsty and sugar was found in the urine. Has had very meager treatment during the past four years. In the past two years has had shortness of breath and swelling of ankles.

**Examination:** Patient rather pale. Eyes slightly prominent. Pulse 108. Apron of fat on abdomen and pads of fat about girdle. Thyroid is small and tough. Large abdominal hernia.



Arteries are rather hard. Heart is not enlarged. Harsh breathing generally over chest, suggesting emphysema. No edema of ankles.

Laboratory: Blood-counts normal. Hemoglobin 70 per cent. Wassermann negative. Blood-sugar 0.24. Urine shows a large amount of albumin, few hyaline and granular casts. Many blood-cells.

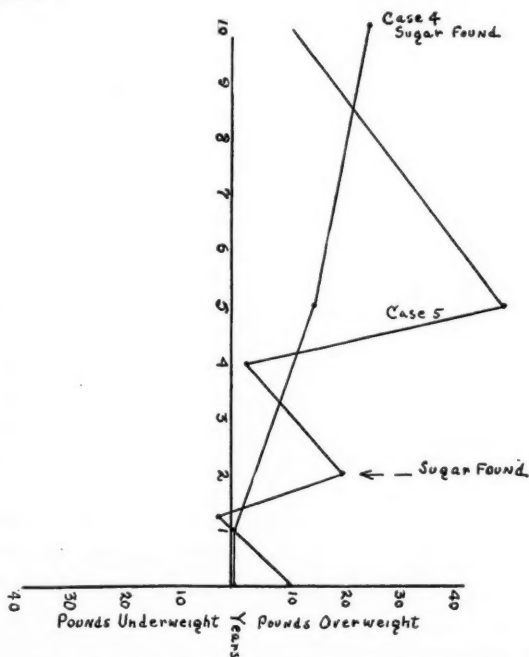


Fig. 283.—Normal weight, Case IV, 139 pounds. Normal weight, Case V, 144 pounds.

Gynecologic consultation: Beginning menopause with menorrhagia.

Course: Patient was put on a 1400 calorie diet (P-50, F-134, Ch-30). Became sugar free under this diet and remained so after increasing the diet to 1800 calories (P-50, F-150, Ch-50). Blood-sugar fell to 0.137.

The weight curve (Fig. 283) as obtained in the history shows a patient with diabetes for ten years who has been overweight until about a year ago, and on examination the weight is found to be just normal. The history correctly predicts what was later found in the hospital, viz., a mild diabetic with a good tolerance.

These are the usual findings with such a history and can be said to be typical of the weight curve of an older diabetic, uncomplicated by infection.

**Case V.**—Medical No. 10,985. A. H., housewife, age fifty-eight. Height 5 feet, 4 inches, weight 161 pounds.

Admitted to hospital in June, 1923, complaining of sugar in urine. One sister died of diabetes and gangrene of leg. Was operated on ten years ago for intestinal obstruction, and twelve years ago for varicose veins. Two years ago began to have aching in muscles of legs and swelling in ankles. Urine was examined and found to contain sugar. Did not have excessive thirst or appetite.

Examination: Overweight with thick panniculus. Physical examination otherwise negative, except for varicose veins of both legs, and partially healed ulcer on left leg. Reflexes not obtained.

Laboratory: Blood-sugar 0.15. Wassermann negative. P. S. phthalein 42 per cent. in two hours. Blood-counts normal. Urine: Very faint trace of albumin and a few hyaline and granular casts.

Course: Was sugar free on a diet of 2000 calories (P-50, F-150, and Ch-150).

This case is included because the weight curve (Fig. 283) shows a very important finding, viz., a gain in weight after the onset of the disease. Sugar was found two years ago, and in the past year patient has gained more than 10 pounds.

It is very important always to ask the patient about gains in weight since sugar has been found. When the patient has gained 10 pounds or more, the disease must necessarily be mild.

**Case VI.**—Medical No. 10,952. D. R., laundryman, age forty-eight. Height 5 feet, 7 inches, weight 107 pounds.

Came into hospital in July, 1923, complaining of weakness. One sister died of diabetes; has always been sickly. Influenza five years ago. Night-sweats following influenza for one month. Over a year ago began losing weight and strength. Always tired. Had polyuria and nocturia; very thirsty. Physician found sugar in urine at this time. Has not followed diet that his physician gave him. Shooting pains in legs for several months and very sore feet.

Examination: Patient rational, but respirations are deep and slow. Skin is dry and scaly—inelastic. Patient is markedly emaciated. There is slight enlargement of the cervical lymph-gland. Marked pyorrhea alveolaris. Chest is very flat. Marked dulness over both uppers. Bronchovesicular breathing over both fronts, more marked on right. A few dry râles at left base, which later disappeared. Definite tenderness in the right upper quadrant of abdomen. Slight resistance to palpation.

Laboratory: Urine shows very strong ferric chlorid reaction. Blood sugar 0.29. Carbon dioxide content 15 volumes per cent. Blood-count: 13,000 leukocytes, of which 77 per cent. are polymorphonuclear. Wassermann negative. P. S. phthalein 55 per cent. in two hours. Later, white blood-cells 5000.

Course: On entering hospital patient was suffering with acidosis and was given 45 units of insulin in the first twelve hours after admission, during which time the blood-sugar fell to normal, but the plasma carbonate remained at 30 volumes per cent. Was given intravenous bicarbonate, after which the plasma carbonate rose to 71 volumes per cent. Patient received during the first ten days of hospital treatment an average of 50 units a day of insulin with a diet of P-50, F-100, and Ch-60. Became sugar free at the end of two weeks on this diet, after which insulin was greatly reduced and the diet increased until discharged from hospital, after seven weeks of treatment, on a diet of P-65, F-230, and Ch-80. Insulin 20 "H" units. Patient's temperature while in the hospital was irregular; at times having a fever as high as 100° F., and at other times being normal. Usually ran a slight afternoon temperature. Tuberculosis complement-fixation test was 2+. x-Ray of the chest

showed increased hilus shadows and dense lung markings. There were localized areas of parenchymatous mottling at the right upper.

This case is presented here as being illustrative of the older diabetic who develops an infection. The physical findings,

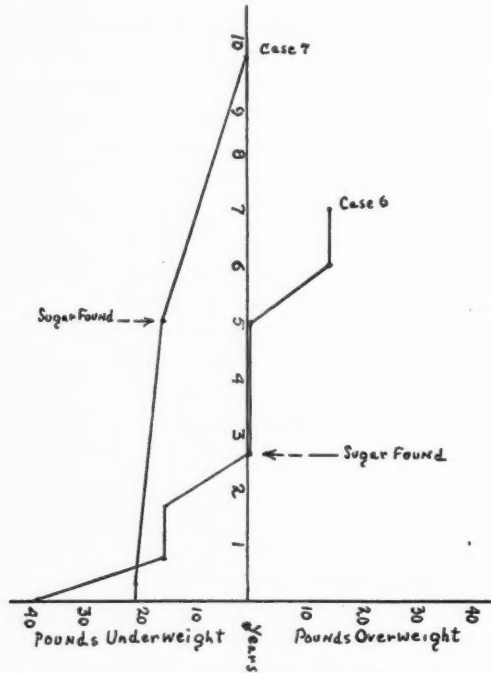


Fig. 284.—Normal weight, Case VI, 156 pounds. Normal weight, Case VII, 167 pounds.

$\alpha$ -ray plate, complement-fixation test, and temperature curve all indicate an active tuberculous process in the lungs. The fact that this man according to the weight curve (Fig. 284) may have had diabetes for two years before sugar was found and maintained a constant weight during that time would suggest that the tuberculosis had a good deal to do with the rapid fall

in weight, which began two and a half years before admission. Excessive carbohydrate feeding also had a good deal to do with this rapid fall. It has been our experience, as stated earlier in the paper, that older diabetics who have such excessively rapid losses in weight usually have some complication of an infectious nature. *At least when a weight curve is obtained which shows such rapid losses in weight one should always look for an infectious disease complicating the diabetes.*

**Case VII.**—Medical No. 11,151. Farmer, age fifty-seven. Height 5 feet, 9 inches; weight 134 pounds.

Admitted to the hospital complaining of weakness and dizziness. No diabetes in the family. Has never suffered a serious illness. Eight years ago had headaches and loss of strength. At the same time thirst became intense and he had polyuria and nocturia.

Examination: Tall man, moderately emaciated. Arteries definitely thickened. Pulsations of arteries of feet could not be felt. Knee-jerks absent. Eye-grounds show a few scattered hemorrhages and one small area of infiltration. Very marked arteriosclerosis of arteries.

Laboratory: Blood-counts normal, except for hemoglobin 75 per cent. Wassermann negative. Blood-sugar 0.27. P. S. Phthalein 60 per cent. in two hours. On a diet of 1400 calories (P-50, F-125, Ch-40) patient averaged 12 to 20 grams of sugar daily. He required 40 units of "H" insulin with a diet of P-60, F-190, and Ch-70. Blood-sugar 0.19.

This case is included because it illustrates an older diabetic with a disease of long duration, who has never been overweight. In the case of an older diabetic who has never been overweight, but steadily loses weight until as much as 20 pounds underweight, one may assume that the disease must be severe. Complications are not apt to be present because the downward course of the weight curve is so gradual. This case shows some diabetic complications, but no infection.

In conclusion, these seven cases have been selected to emphasize points enumerated at the beginning of the paper:

Case I, a young diabetic running a rapid downward course.

Case II, a young diabetic, not severe, whose loss in weight depends on his occupation.

Case III, a young individual, having glycosuria, but not diabetes.

Case IV, an older diabetic, who has lost 25 pounds, yet remains a mild case.

Case V, a still milder diabetic, showing gains in weight after acquiring the disease.

Case VI, an older diabetic, whose rapid downward course is associated with a serious complication—tuberculosis of lungs.

Case VII, an older diabetic, always underweight, showing a steady but slow loss of weight for ten years, which in itself suggests a severer form of the disease than is customary at his age.

## CLINIC OF DR. ALPHONSE McMAHON

ST. JOHN'S HOSPITAL

### PURPURA

**Melena, Hemoptysis, and Menorrhagia Occurring with Purpura in Two Cases. Discussion of the Infectious Nature of Purpura Hæmorrhagica and Acute Leukemia. The Difficulty of Differential Diagnosis. Calcium Therapy in Hemorrhagic Diseases.**

THIS afternoon we will discuss the subject of purpura. While much has been written in an attempt to classify the sign or to establish it as a separate disease entity, it must still be discussed as a symptom or a sign of some intoxication or infection about the body, or as due to one of the many other states which have served as etiologic factors. Its clinical identity has not been clearly established. Much confusion exists as to the proper classification of this sign. There is a broad group of cases characterized by a purpuric rash whose etiology has not been determined, the so-called idiopathic purpuras. These have been subdivided into types expressing fairly definite clinical pictures, varying in severity, but which etiologically are probably identical.

The subdivision of the idiopathic purpuras commonly accepted has been: (1) Purpura simplex, described by Zeller in 1684, characterized by cutaneous hemorrhages, with few constitutional symptoms. (2) Purpura rheumatica, or peliosis rheumatica, the so-called Schönlein's disease, in which cutaneous hemorrhages are associated with joint symptoms. (3) Purpura hæmorrhagica (morbus maculosus werlhofii, 1775). This is the most severe of the three, with hemorrhages not only into the skin but also from the mucous and serous membranes about the body. (4) Henoch's purpura, occurring chiefly in children,

characterized by the gastro-intestinal crises of abdominal pain, vomiting, and diarrhea, with dermal hemorrhages.

While the clinical entities described are apparently separate and distinct, their close resemblance to one another makes it appear that the etiologic factor in all is the same, and their difference is one of degree and not of kind.

**Case I.**—The following case history is cited to show the classical manifestations of a severe type, and also to add certain facts to the etiology of cases presenting the sign purpura.

Mr. E. H., aged eighteen, referred by Dr. E. H. Reuss, Granite City, Ill.

*Present History.*—The chief complaints on entrance are: (1) Melena; (2) hemoptysis; (3) skin eruption, general over the body; (4) malaise and anorexia; (5) elevation of temperature.

*Duration*, three weeks.

*Course.*—The onset was sudden, with painful swelling of the knees, ankles, and elbows. With this, a maculopapular eruption appeared, localized chiefly about the knees. Two weeks before the onset the patient had complained of a mild sore throat.

*Progress.*—The swelling of the joints became pronounced, with the appearance of pain on motion. The maculopapular eruption spread very quickly to the extremities and trunk, papules rapidly become vesicles, fusing to form larger blebs, containing a serosanguineous fluid. Gastro-intestinal symptoms appeared two days after this, characterized by nausea and persistent vomiting, followed almost immediately by severe diarrhea, with the passage of frequent bloody stools. Bleeding from the buccal mucous membrane and hematuria appeared at about the same time. The swelling and pain in the joints gradually subsided, but the bleeding from the mucous membranes persisted. Bleeding from the bowels frequently occurred independently of bowel movements. On the day before entering the hospital the patient fainted, following the last of five hemorrhages from the bowels. The purpuric rash subsided, together with the other symptoms, until two days before entrance, when



the patient had evidence of new patches, more diffuse about the extremities and trunk, the eruption varying from maculæ to severe bullæ. The patient gives a history of having been treated for *Oxyuris vermicularis* infestation shortly before entering the hospital.

*Past History.*—Usual childhood diseases, no sequelæ. Tonsils and adenoids removed at the age of four, followed by intermittent fever, exact nature of which was not determined. During later childhood and early adult life the patient was free from all disease until the age of fifteen, at which time he had an attack similar to the present, with purpuric rash and joint symptoms, but without the severe bleeding from the mucous membranes. This lasted about two months. No history of injuries or operations. No symptoms referable to other systems. *Personal:* Negative throughout. *Venereal history* negative. *Family:* Negative for constitutional illnesses or any history of purpura.

*Physical Examination.*—The patient is well developed and fairly well nourished, showing evidence of moderate loss of subcutaneous tissue and pronounced pallor of the skin and mucous membranes. Pulse, 120. Respiration, 28. Temperature, 101° F. *Dermatologic consultation* (report of Dr. Jos. Grindon, St. Louis): The lesions on the back and abdomen consist chiefly of stains from 2 mm. to 2 cm. in diameter. Some of these show central areas, probably the sites of bullæ. About the elbows are the same macules and papules, undergoing retrogression. The active part of the eruption now extends from the hips to and including the feet, consisting of blood-stained bullæ  $\frac{1}{2}$  cm. or less in diameter, and some smaller macules, the latter not distinctly hemorrhagic. Some deep bullæ are present on the soles. The lesions are not definitely grouped over the joints, except at the elbows. Over the left popliteum, where tincture of iodine was painted, the lesions are confluent and sharply limited to the area of application. No itching. The patient describes a similar eruption four years ago during an attack of joint pains. He states that the eruption at that time was not preceded by any internal medication. *Regional*

*examination*—*Head*: No evidence of purpuric rash on the scalp. *Ears*: Purpuric spots, papular in character, along the outer borders. Hearing normal. *Eyes* negative. *Nose*: No bleeding spots on the mucous membranes. *Mouth*: Distinct pallor of the mucous membrane of the lips and cheeks; gums fairly firm, without evidence of bleeding at this time. Small area of ulceration on the soft palate, to the left of the midline, irregular in outline, with grayish-white base and slight serous exudation. *Neck*: Thyroid negative. Few small glands palpable in the posterior cervical chains. (Axillary glands palpable, slightly tender; epitrochlears negative; inguinals palpable.) *Chest* negative. *Heart*: Apex impulse in the fifth interspace, within the mammillary line, diffuse, not heaving in character. Sounds at the apex rapid, synchronous with pulse. Rate 120. Soft systolic murmur at the apex, more intense in the second pulmonary area, disappearing on deep inspiration, of functional type. Blood-pressure, 132/80. *Abdomen*: Asthenic type, no tumefactions or visible peristalsis. No tenderness or rigidity on light palpation. Tympany throughout. *Liver* border palpable  $1\frac{1}{2}$  cm. below the costal margin, in the mammillary line, slightly tender. *Gall-bladder* region negative. *Spleen* definitely enlarged to percussion, but not palpable at this time. *Kidneys* not palpable. *Colon* normal throughout, except for tenderness over entire viscus. *Rectal*: Slight dilatation of the external hemorrhoidal veins, but no bleeding. Soft mass palpated in the rectum, consisting of clotted blood. Prostate and seminal vesicles negative. *Extremities*: Both knee-joints enlarged and prominent, but not tender on movement. Some tenderness on pressure over both ankles, with very slight edema. *Reflexes*: No pathologic toe reflexes. Other reflexes normal throughout.

*Radiographic*.—Stereoscopic radiograms of the chest reveal some peribronchial infiltration in the upper right lung, with evidence of thickening of the pleura, probably old, about the middle fissure. No other evidence of lung or chest pathology. *Fluoroscopic*: Chest negative.

*Laboratory*.—Erythrocytes, 2,860,000; leukocytes, 17,600; hemoglobin, 25 per cent. *Clotting time*, three minutes, fifteen sec-

onds. *Blood grouping*: Group II (Moss classification). *Differential count*: Polymorphonuclear leukocytes, 77 per cent.; eosinophils, 2 per cent.; large lymphocytes, 1 per cent.; small lymphocytes, 17 per cent.; myelocytes, 2 per cent.; transitionals, 1 per cent. *Blood-smear* negative for plasmodia. *Feces*: Positive blood macroscopically, with ova and parasites negative. *Wassermann* negative. *Widal* negative. *Urine* (catheterized specimen): Definite trace of albumin, leukocytes 10 and erythrocytes 15 to the high-power field, numerous hyaline and granular casts. *Phenolsulphonephthalein test*: 47.5 per cent. of dye eliminated in two hours. *Blood-cultures* repeatedly negative.

*Progress*.—A diagnosis of purpura hæmorrhagica was made. Owing to the extreme loss of blood, with marked weakness, it was thought advisable to transfuse the patient immediately. Citrated blood 500 c.c. was given intravenously, with marked improvement in the general condition. Bleeding from the bowels persisted, however, together with hematuria, although there was an increase in the number of erythrocytes, with elevation of the hemoglobin, on the following day, the erythrocytes being 3,240,000; the hemoglobin, 30 per cent.; the leukocytes, 16,800; the clotting time, three minutes, thirty seconds. The usual hemostatic treatment was given, in the form of calcium lactate in 15-grain doses (every three hours), together with hemoplastin\* 1 c.c. subcutaneously daily. Later, sodium salicylate and sodium bicarbonate, 15 grains of each every four hours, were administered to control the joint pains. The patient continued to run a slight temperature for several days, with gradual decrescence. The bleeding continuing, a second transfusion was given forty-eight hours after the first, and the third transfusion, seventy-two hours after the second. Under this treatment there was recession of the purpuric areas, with no evidence of new patches. The red count increased from 2,860,000 at the original count to 4,240,000 before dismissal. The hemoglobin increased from 25 per cent. at entrance to 75 per cent. on dismissal, the leukocytes dropping from 17,000 to 7100. There was constant variation in the leukocyte count, the highest

\* Parke, Davis & Company, equine and bovine sera.

point reached occurring two days after entrance into the hospital, when it was found to be 22,400. Following this the count remained for several days at about 16,000 to 17,000, gradually dropping to a final count of 7100. With recession of the purpuric spots, there was gradual cessation of the bleeding from the bowels. The hematuria persisted, however, together with leukocytes, hyaline and granular casts, and occasional waxy casts in the urine. Ten days after entrance into the hospital edema of the ankles developed, gradually progressing to a moderate degree of anasarca, associated with a decrease in the urinary output. The albumin increased to 4 gm. per liter, with an increase in all microscopic findings. The two-hour phthalein excretion was reduced to 25 per cent. (from 47.5 per cent. on entrance), the patient developing all signs of an acute nephritis. The blood-pressure at this time was found to be 132/80, and taken daily showed no elevation above this point. Under observation the albumin increased to 10 gm. per liter, but following treatment this was gradually reduced, so that when the patient left the hospital the urine showed 5 gm. of albumin per liter, with numerous erythrocytes and hyaline and granular casts. The edema had cleared up and the patient's general condition was markedly improved, with very slight evidence of the eruption, in the form of desiccated bullæ, while the smaller purpuric spots had disappeared completely, leaving numerous copper-colored patches about the lower extremities. There was no evidence of bleeding from the mucous membranes, and no new purpuric areas had been observed in the course of treatment. During the entire course the patient was kept on the treatment outlined above. Early in the course of the illness fluids were forced, the patient taking 3 to 4 liters a day, with orange albumin. Later, with the development of the acute nephritis, the fluids were restricted. The pulse and temperature were normal on dismissal.

*Discussion.*—Purpura has been found associated with many clinical conditions. The following classification embraces most of the known causes: (1) Infections—tuberculosis, nephritis, malaria, typhoid, exanthemata, septicemias (staphylococcus,

streptococcus, meningococcus). (2) Cachexias—senility, malnutrition, carcinoma, sarcoma. (3) Blood states—leukemias, pernicious anemia, aplastic anemia. (4) Nervous diseases—tabes, syringomyelia, myelitis. (5) Intoxications—(a) drugs—iodin, ergot, quinin, bromids, arsenic, copaiba, belladonna, mercury, benzol<sup>1, 3</sup>; (b) biologic (vaccines, sera, etc.)—diphtheria toxin,<sup>1</sup> tuberculin,<sup>1</sup> antiplatelet serum.<sup>2</sup> (6) Mechanical conditions—trauma, stasis, embolism.

The intensity of the pathologic manifestations depends upon the severity of the exciting cause. For example, in the infectious type of case the more virulent the infection occurring in an individual with a tendency toward purpuric manifestations, the more pronounced is the purpura.

Many observers have attempted to isolate specific infecting organisms in these cases. Kolb, Burch, and Letzerich<sup>4</sup> described an identical bacillus with which they have succeeded in producing the malady by inoculations in animals. Jacobson<sup>5</sup> reports a case in a child five and one-half years of age from whose blood the *Streptococcus hemolyticus* was isolated in pure culture. Injections of the culture into experimental animals failed to produce the disease.

Regarding the pathogenesis of this condition many theories have been suggested, such as fragility of the capillaries, capillary embolisms, changes in the blood, and the action of toxi-infectious agents. Duke<sup>1</sup> has shown that in these cases the blood presents the following changes: (1) Reduction of blood-platelets; (2) normal coagulation time, and (3) prolonged bleeding time. Minot<sup>6</sup> in an exhaustive article on purpura hæmorrhagica concludes that the low platelet count is due to one or both of the following facts: Either some reaction, presumably a specific poison, taking place in the body destroys the platelets as fast as they are formed, or there is a localized aplasia of the platelet-forming elements of the marrow due to some toxic phenomenon.

In the case cited herewith the infectious element seems to prevail, placing the case in the category of infectious purpura, although no infecting organism was isolated from the blood

on repeated culture, and none was obtained on culture of the blebs. The clinical course of the case is one of infection, in the order of pharyngitis or tonsillitis, purpura, and nephritis. The etiologic factor producing the tonsillitis we feel is identical with that producing the purpura and the nephritis. Further facts to substantiate the idea of infection are the fever and leukocytosis. The late appearance of the renal decompensation is interesting, inasmuch as the patient showed definite signs of renal involvement on entrance, and with normal renal function, these findings were considered as a part of the purpuric picture. They were actually a forerunner of the decompensation which followed, and the nephritis may be said to have been present concurrent with the purpuric rash.

It may be necessary at times to differentiate the so-called idiopathic purpura hæmorrhagica from aplastic anemia and aleukemic lymphatic leukemia with severe purpuric manifestations. The differentiation on the basis of bone-marrow changes has been discussed by Falconer and Morris.<sup>7</sup> The marrow of aplastic anemia is fatty throughout, devoid of small islands of hematopoietic tissue. Aleukemic leukemia presents a marrow with marked hyperplasia of the lymphoid elements, while the marrow of the long bones in (idiopathic) purpura hæmorrhagica is more cellular than that in the aplastic anemia and may be slightly reddish, depending upon the degree of activity. Clinically, they may be differentiated by the fact that the aplastic anemia shows a marked anemia and secondary purpura, stomatitis, and febrile reaction as common symptoms. The spleen is not enlarged, and there is no adenopathy. Aleukemic lymphatic leukemia presents a clinical picture of anemia, purpuric hemorrhages, fever, and stomatitis, more frequently with an enlarged spleen and local or general glandular enlargements, although many cases do not present these last two. It is questionable whether there is any specific different pathologic marrow for each type of purpura. In purpura hæmorrhagica the anemia is not as marked as in aplastic anemia, while the marrow activity, as evidenced in the blood-smear by the increase in percentage of reticulated red cells, nucleated red cells, and poly-

chromatophilia, is more pronounced. The spleen and lymph tissues ordinarily are not involved.

*Treatment.*—The specific treatment is based upon the etiology of the condition, while, of course, the symptomatic treatment is the same for all and applies likewise to other hemorrhagic syndromes. Drug intoxications must be eliminated, local and systemic infections treated as indicated, and mechanical conditions removed. In the symptomatic treatment we seek to replace the platelets and to stimulate the marrow to produce new platelets. The decrease of platelets, according to Duke, is responsible for the prolonged bleeding time. Other elements concerned in the clotting of the blood, chiefly thromboplastin and calcium, are supplied. Platelets are replaced by transfusions of whole or citrated blood. This may be done by any of the methods in common use. Subcutaneous or intramuscular injections of whole blood or serum, either human or animal, in doses of 20 to 40 c.c. every four to six hours, have given positive results, and by many observers are considered to be of more distinct value than the intravenous method.

The case cited above was given three transfusions of citrated blood of 500 c.c. each, with distinct improvement following all transfusions, and later a complete cessation of bleeding, with no new purpuric spots after entrance into the hospital. Citrated blood in this type of case has been found to give good results rather constantly, so that the employment of the direct method of transfusions, the indirect whole blood method, or the subcutaneous or intramuscular injections of whole blood or serum has not seemed to be absolutely necessary, although in the case to be discussed later this last method was employed in conjunction with transfusions of citrated blood.

There should be no hesitation in the employment of the transfusions in cases where the symptoms are severe. They should be repeated at frequent intervals, at least every twenty-four to forty-eight hours, until a decided response is obtained, manifested chiefly by a cessation of the bleeding into the skin or from the mucous membranes. The necessity for continuance of the transfusions should be based not solely upon the platelet



count, for this is not always a satisfactory determinant; the persistence of bleeding is a much more reliable indication.

The coagulant substances used are numerous, consisting of sera, tissue emulsions, or extracts of blood-platelets. The two most commonly used are thromboplastin\* and hemoplastin. Hemoplastin was used in this case in 1 c.c. doses, given daily. It has been of definite value in cases of prolonged clotting time, hemophilias, etc., and would not seem to be indicated in these cases of purpura with normal clotting time. Yet in spite of the normal reports regarding the thrombokinase, prothrombin, and calcium content of the blood in these cases, the use of some of these substances appears justified by the results obtained. Calcium salts have been used to decrease both bleeding time and clotting time. Their specific value in purpura may rest in the fact that they tend to "close the cells of the capillary walls," thus preventing the excessive bleeding, which is not, as we have seen, due to an increase in the clotting time. Calcium lactate and calcium chlorid have been the salts most frequently employed. It is necessary to administer these drugs in larger doses than ordinarily recommended. It is questionable whether they are effective when administered orally, and surely 5-grain doses every three or four hours are of extremely doubtful therapeutic value. They should be given in doses of 30 to 60 grains, or even more, every three to four hours. Calcium chlorid has been used intravenously by different observers. Pottenger<sup>8</sup> has recommended the use of calcium in many conditions where parasympathetic action is dominant, *e. g.*, anaphylactic states, urticaria, asthma and the related hay-fever, bronchitis, and various affections of the gastro-intestinal tract. Afenil† is a preparation of calcium chlorid, the soluble albuminate of the salt, 10 per cent., which is put up in ampule form, each ampule containing 10 c.c. of the 10 per cent. solution. This makes it

\* Squibb & Company, derived from ox-brain, in accordance with the method of Dr. F. Hess, of the Research Laboratory of the New York Department of Health. This contains kephalin and other thromboplastic substances of cerebral tissue which are essential to normal blood-clotting.

† Knoll & Company, Ludwigshafen, A. R.: Germany (Agents, E. Billhuber, New York). Chlorcalcium carbamid, 10 per cent. solution.



very convenient for general use, but according to our observations it is no more effective than the simple salt. It is usually given in daily 10 c.c. doses intravenously until the condition improves. The relation of the parathyroid to calcium metabolism, as determined chiefly in tetany, suggests the use of parathyroid substance whenever calcium is used in an effort to increase the cellular absorption of the calcium ions. This is given in  $\frac{1}{2}$  to 1 grain of desiccated substance four times a day.

In conclusion, treatment must be vigorous and all methods which may increase the number of platelets or assist in any way in hemostasis should be employed intensively enough to effect results.

**Case II.**—The next case history to be discussed is that of a girl aged fifteen, presenting the chief symptom of menorrhagia, with bleeding from the mucous membranes of the nose and mouth, associated with purpura. The contrast between the preceding case and this case is seen chiefly in the constitutional reaction to the specific cause producing the purpura, together with other facts relative to the blood state.

Miss V. D., aged fifteen, referred by Dr. E. H. Reuss, Granite City, Ill. The patient entered the hospital June 24, 1923, complaining of (1) menorrhagia, (2) bleeding from the nose and mouth, (3) eruption over the lower extremities, from knees to ankles, and (4) weakness and fatigability. *Duration*, twelve days. The onset was sudden, associated with the onset of the menstrual period, twelve days before entrance. There was no history of bleeding before one year ago, at which time the nasal hemorrhages appeared, occurring cyclically with the menses, lasting from four days to one week, the duration of the menses. Four months ago the menorrhagia appeared for the first time, the patient flowing profusely for about seven days, passing large clots. At that time there was evidence of nasal hemorrhage and bleeding from the gums. No purpuric spots were noticed. Extreme weakness followed each menstrual period. The menorrhagia, with bleeding from the nose and mouth, has recurred with each period to the present time. *Progress:*

The present attack started with the period twelve days ago, with profuse bleeding. Immediately preceding this there has been no evidence of bleeding from any mucous membrane. Soon there appeared bleeding from other mucous membranes about the body, particularly the gums. This bleeding has continued to the present time, with practically no recession of the vaginal bleeding, and with a gradually progressive weakness and extreme fatigue. Purpuric spots appeared about four days before entrance into the hospital, small, discrete areas, varying in size from 2 to 6 mm., of maculopapular type, without any tendency to bleb formation. There has been no history of melena, hematemesis, or stomatitis in association with this present attack.

*Past History.*—Double pneumonia at three months of age. Mumps, measles, and diphtheria as a child, without sequelæ. The patient was treated for anemia at the age of seven. No operations, no injuries. No history of the present condition before the time mentioned above. *Personal:* Negative. *Menstrual:* Onset of the menses at thirteen, regular, twenty-eight-day type, with moderately profuse flow, black in color, with very disturbing odor. No dysmenorrhea until the past four months, this occurring concomitantly with the menorrhagia. *Family:* No history of constitutional illnesses. No purpura in any of the ascendants or immediate family.

*Physical Examination.*—Reveals a poorly nourished white female of normal development, showing marked pallor of the skin and mucous membranes, an apathetic expression, slight restlessness, and evidence of gingival bleeding. Petechiæ are seen about the legs from knees to ankles, varying in size from 2 to 6 mm., discrete, with no tendency to confluence or vesiculation. *Regional—Head:* No evidence of purpuric rash. *Ears* negative. *Eyes:* Pupils equal, reaction normal. *Nose:* Definite bleeding from both nostrils, more marked on the right. Blood-soaked gauze pack in the right nostril at this time. *Mouth:* Some difficulty in opening the mouth and separating the teeth, the patient complaining of slight stiffness in the articulations of the jaw. Mucous membranes of the lips and

cheeks showing definite pallor, pharynx injected. Some oozing from the tonsils, marked oozing from the gums. *Neck:* Cervical glands negative (axillary and epitrochlear glands negative). *Chest* negative. *Heart:* Impulse in the fifth interspace, within the nipple line, rapid, diffuse. Rate, 140. Sounds rapid, but normal in character. Pulse low volume and tension. Blood-pressure, 106/48. *Abdomen* negative throughout. Liver not palpable or tender. Spleen not enlarged to palpation or percussion. *Vaginal:* Thick sanguineous discharge from the vagina, consisting of free blood and numerous clots. Uterus normal in size and position, freely movable. No pelvic pathology. *Rectal:* Negative. *Extremities:* Petechiæ, as mentioned above. *Reflexes* normal.

*Laboratory.*—Erythrocytes, 3,600,000; leukocytes, 7800; hemoglobin, 70 per cent. *Differential count:* Neutrophilic leukocytes, 69 per cent.; basophilic, 1 per cent.; eosinophilic, 1 per cent.; large lymphocytes, 12 per cent.; small lymphocytes, 10 per cent. *Clotting time*, over fifteen minutes. *Blood group* III (Moss classification). *Blood-smear* negative for plasmodia. *Wassermann* and *Widal* negative. *Urine:* Medium trace of albumin, dextrose negative, microscopic negative. Repeated *blood-cultures* negative.

*Course in the Hospital.*—Shortly after entrance the patient was given a transfusion of citrated blood, 500 c.c., with a slight improvement in the general condition. Hemostatic medication employed consisted of calcium lactate 15 grains every three hours, hemoplastin 1 c.c. daily, and afenil 10 c.c. intravenously daily. Although the bleeding showed some cessation following the transfusion, there was very little change in the erythrocyte count and no change in the clotting time. The hemoglobin remained the same. The second transfusion was done four days after entrance, at which time the erythrocyte count was 3,544,000 and the clotting time over fifteen minutes. The general response following this second transfusion was not so pronounced as with the first, although there was an elevation in the erythrocyte count to 3,620,000 and the first reduction in the clotting time, the time then being ten minutes and

forty seconds. The bleeding still continued. Following a gynecologic consultation with Dr. William H. Vogt, St. Louis, the patient was placed upon ergot intramuscularly and by mouth, with a slight reduction in the vaginal bleeding. Throughout the course of the illness there was no appreciable change in the vaginal bleeding. A reduction one day would be followed by an increase the following day. However, there was a progressive reduction in the clotting time, which one week after entrance was nine minutes, the erythrocytes being 3,580,000 and the hemoglobin remaining at 70 per cent. Three days after the second transfusion whole blood was given intramuscularly, 20 c.c. daily. It was following this that the first appreciable drop in the hemoglobin was noted, this being reduced to 50 per cent. (Sahli), the clotting time then being five and a half minutes. The hemoglobin continued to descend, with a drop in the erythrocyte count, so that on July 3d it was found to be 35 per cent., with an erythrocyte count of 3,100,000 and a clotting time of five and a half minutes. Myocardial weakness became pronounced with the progress of the illness, and on July 5th the hemoglobin was found to be 25 per cent. and for the first time the leukocytes were found to be increased in number, being 76,800, with the differential count as follows: Polymorphonuclear leukocytes, 64 per cent.; eosinophilic, 3 per cent.; large lymphocytes, 5 per cent.; small lymphocytes, 4 per cent.; myelocytes, 12 per cent.; basophils, 2 per cent.; eosinophils, 1 per cent.; transitionals, 2 per cent.; nucleated red cells, 7 per cent. The spleen was not palpable and there was no appreciable adenopathy. The uterine bleeding increased slightly. The patient became delirious and died within a few hours.

*Discussion.*—The onset of this case is interesting in many particulars, chief among which is the history of menorrhagia for four months preceding the onset of the acute leukemia. The purpuric rash, which was not extensive, was rather a late development, occurring not two weeks before the death of the patient. Menorrhagia in hemophilias and purpuras is not unusual, but its occurrence as a sign in acute leukemias, in association with bleeding from the other mucous membranes, is not stressed in the literature. Minot<sup>6</sup> cites a case of purpura

hæmorrhagica with menorrhagia. Comparison of the above two cases reveals the fact that the latter shows a distinct increase in coagulation time, while the former has a perfectly normal coagulation time. It is to be noted also that, with the reduction in clotting time, there is very little change in the erythrocyte count or the hemoglobin.

The leukocyte counts were normal on admittance to the hospital, establishing one essential point, in the diagnosis of a proved case of acute leukemia, which is an aleukemic or a sub-leukemic stage (Gorham<sup>9</sup>). Other points necessary for a proved case, according to the same author, are: (2) an acute downward course, with death, usually ensuing in from one to four months; (3) the characteristic blood-picture of myeloblasts and myelocytes, with transition forms between the two; (4) the typical gross and histologic findings of the liver, spleen, bone-marrow, and lymph-glands, and (5) the specific proof of myeloid elements by enzyme reactions. Aside from the positive pathologic findings, as no autopsy was permitted, this case also satisfies the other demands for a proved case of acute myelogenous leukemia. Until the appearance of the increased leukocyte count, with the differential findings of a myelocytosis, an etiologic factor for the bleeding could only be surmised. There was absolutely no history of preceding infection in this case, such as we have found in the case of purpura hæmorrhagica cited above. Although the case, in common with others, presented symptoms definitely suggesting infection as a basis for the leukemia, such as fever, etc., the absolute proof could not be established. The weight of general evidence in regard to the etiology of the acute leukemias seems to be in favor of the infectious theory, for blood-pictures comparable to those seen in the leukemias have frequently been observed in acute infections of known etiology. In fact, the distinction between the two diseases may lie solely in the outcome (Pappenheim et al.<sup>9</sup>).

The bleeding occurred only cyclically, at the time of the normal menstrual period, first with epistaxis and later with excessive uterine bleeding. While bleeding from the gums was present on admission, there was no evidence of a true stomatitis,

as has been reported in numerous cases of acute myelogenous leukemia (Billings and Capps,<sup>10</sup> David L. Edsall<sup>11</sup>). It is well to bear in mind that acute leukemias often present as one of the first symptoms a stomatitis, frequently becoming gangrenous, and the relation of its development to the extraction of teeth has been noted by many observers. The evidence all points to the precedence of the myelogenic infiltration, producing the local dental symptoms, leading to extraction, and not vice versa. All cases presenting symptoms of stomatitis, with or without the associated symptom of purpura or mucous membrane bleeding, should have blood-smears carefully examined for the presence of abnormal marrow cells. Billings (1903) states that a differential diagnosis between acute myelogenic and acute lymphatic leukemia cannot be made by the clinical symptoms, physical signs, or ordinary count of the white cells. The type can be identified only by differentiating the types of white cells in the same specimen. He sums up the blood-picture of acute myelogenic leukemia as follows: (1) Anemia, progressive and severe; (2) increase in the white blood-corpuscles, 16,000 to 540,000; (3) a large proportion of the white cells, 25 to 96 per cent., made up of myelocytes, large mononuclear cells of the same size, and faintly granular large mononuclear cells (transitional cells), and (4) eosinophils, mast cells, and nucleated red corpuscles may be absent or present in varying numbers.

The cell identity must be established to differentiate the two conditions. The cell which has prompted much discussion is the mononuclear form, which is found in both types of cases. In the past confusion existed as to the exact nature of this cell, whether myeloid or lymphoid, and the isolated cell may still present difficulties. It is here that the oxydase reaction of Winkler<sup>12</sup> has proved of definite value. With this stain all the cells of myeloid origin will show blue granules. However, in a given blood preparation with numerous mononuclears present, associated with premyelocytes and myelocytes, it is safe to conclude that the mononuclears are myeloblasts. The predominant cell characterizes the type of leukemia.

*Treatment.*—The treatment in this case varied little from

that described for the purpura hæmorrhagica, with this exception, that intramuscular injections of whole blood, from 20 to 30 c.c., were used daily in conjunction with the transfusions of citrated blood. With these, hemoplastin was given in 1-c.c. doses daily, with calcium lactate 15 grains every three hours. Afenil was given in 10-c.c. doses intravenously each day. Under this medication the coagulation time of the blood was reduced from over fifteen to four minutes (in the last observation). This reduction of coagulation time did not, however, materially influence the bleeding.

A point of interest in this case was the rapid decline, with death shortly following the appearance of the myelocytosis. This type of case has a usual duration of from one to four months. The fatal outcome is characteristic and serves to establish positively a diagnosis based upon an atypical blood-picture.

#### BIBLIOGRAPHY

1. Duke: Arch. Int. Med., vol. xi, 1913.
2. Lee and Robertson: Jour. Med. Res., 1916, 33, 323.
3. Anderson, Boyd, and Jackson: Canad. Med. Assoc. Jour., vol. xiii, No. 6, 1923.
4. Quoted by Jos. L. Miller: West Virginia Med. Jour., vol. xv, No. 10, April, 1921.
5. Jacobson: Urol. and Cut. Review, vol. xxv, No. 6, June, 1921.
6. Minot: Amer. Jour. Med., Sci., 152, 1916.
7. Falconer and Morris: Clin. of North Amer., vol. vi, Pt. 1, 1922.
8. Pottenger: Ann. Clin. Med., vol. ii, November, 1923.
9. Gorham: Albany Med. Ann., 38, 1917.
10. Billings and Capps: Amer. Jour. Med. Sci., 126, 1903.
11. Edsall: Amer. Jour. Med. Sci., 130, 1905.
12. Winkler: Folia Hemat., iv, 323, 1907.

#### ADDITIONAL BIBLIOGRAPHY

##### PURPURA

1. Hawes, John B., 2d: Boston Med. and Surg. Jour., vol. 161, No. 15, 1909.
2. Duke: Jour. Amer. Med. Assoc., vol. 55, No. 14, 1910; Jour. Exper. Med., vol. 14, 1911.
3. Drinker and Hurwitz: Arch. Int. Med., vol. 15, 1915; Jour. Exper. Med., vol. 21, 1915.
4. Anwyl-Davies: Boston Jour. Dermat. and Syphil., vol. 33, 1921.
5. Herrmann: Med. Clin. of North Amer., March, 1923.
6. Larrabee: Jour. Amer. Med. Assoc., vol. lxxx, No. 11, March 24, 1923.
7. Service: Clifton Med. Bull., vol. 9, No. 3, 1923.

## LEUKEMIA

1. Cheney: Med. News, 85, 1904.
2. Dock and Warthin: Med. News, 85, 1904.
3. Beifeld: Arch. of Diag., 8, 1915.
4. Ward: Brit. Jour. Child. Dis., 14, 1917.
5. Peabody: Boston Med. and Surg. Jour., vol. 177, No. 25, December 29, 1917.
6. Fitz: Jour. Amer. Med. Assoc., vol. 75, No. 20, November 12, 1920.
7. Maynard: Jour. Amer. Med. Assoc., vol. 76, No. 4, January 22, 1921.
8. Barker: Southern Med. Jour., vol. xiv, No. 6, June, 1921.
9. Schisler: Med. Record, vol. 99, No. 13, March 26, 1921.
10. Theobald: Lancet, September 2, 1922.
11. Moore, Sir John W.: Irish Jour. Med. Sci., January, 1923.
12. Ketron and Gay: Arch. Dermat. and Syphil., vol. 7, No. 2, February, 1923.
13. Foot and Jones: Amer. Jour. Dis. of Child., vol. 25, No. 5, May, 1923.



## CLINIC OF DR. LOUIS HENRY HEMPELMANN

EVANGELICAL DEACONESS HOSPITAL

### MIKULICZ'S DISEASE

THE patient I am presenting today is a married woman, thirty-nine years of age. Family history: Father died of cancer of the tongue; mother alive and well. Previous history: Has always enjoyed good health. Has had four living, healthy children. No history of miscarriages. Menses regular. Present trouble: The patient came under observation first in February, 1923, at which time she stated that she had had recurrent severe attacks of epistaxis for two months. She also had an abscess of the right elbow. The abscess was incised and about 3 ounces of pus evacuated, after which it healed without difficulty. Nasal examination failed to show any bleeding point or ulceration, and packing and the use of thromboplastin, horse-serum, etc., giving no permanent relief, she was finally given a citrate transfusion of 500 c.c. of blood, which brought about a great improvement in her condition and cessation of the hemorrhages. The blood-count before the transfusion was: red blood-cells 1,220,000, hemoglobin 30 per cent., white blood-cells 1300. Examination of the smear showed no marked irregularity in size or shape of the red blood-cells, no poikilocytosis, no nucleated reds. There was, however, a relative increase in the lymphocytes. The lacrimal and salivary glands were normal at this time, as were also the lymphatic glands.

After a stay of some three weeks in the hospital, she returned to her home in the country. For three months she remained tolerably well. Then she noticed a swelling of both parotids and began to have a slight elevation of temperature. The attending

physician at first thought it a case of mumps; later, however, sent her to the hospital as she showed no signs of improvement. She re-entered the hospital on May 24th. At this time there was a general enlargement of both parotids, both submaxillary and sublingual glands. The postcervical glands were only slightly enlarged, much less than at present, and the induration of the skin was not present. This developed about two weeks ago and has been spreading rather rapidly. The patient has had an evening rise of temperature varying from 99° to 101° F. since being under observation. The morning temperature, as a rule, has been normal.

**Physical Examination.**—You will note at once the peculiar enlargement of both parotids which resembles that seen in mumps. On closer inspection, however, you will see that both lacrimal glands are also enlarged causing the upper lids to project over the eyes. There is also a peculiar thickening of the skin extending from the right temporal region over the forehead almost to the midline. It terminates in a sharp, well-defined margin which is distinctly elevated over the normal skin. A similar induration of the skin is present on the right side of the chin. This indurated skin is firm to the touch and feels definitely thickened and "brawny." You will also note that the cervical lymph-glands are enlarged and project above the level of the normal skin, and on raising the chin an enlargement of the submaxillary glands on either side is evident. The other lymph-glands, such as the axillary, inguinal, and epitrochlears, are not enlarged. The tonsils are normal. The patient is well nourished, but the color is rather pasty, such as one sees in old nephritics. The heart and lungs are normal; the spleen is slightly enlarged and has grown perceptibly in size since the patient has been under observation, viz., four weeks. The pupils are active, reacting normally to light and accommodation, and the deep reflexes are normal. Her strength is fairly good and there are no disturbances of sensation or of the special senses. The blood-pressure is 115/65. Urinalysis: 1.010, acid, faint trace of albumin, no sugar; microscopic—negative. The blood examination on May 24th when she re-entered the hos-

pital showed a leukopenia with a relative increase in the small lymphocytes, viz., red blood-cells, 4,616,000; white blood-cells, 2700; hemoglobin, 89 per cent. (Dare).

Differential count.	May 24th.	June 7th.	June 24/23.
Number white blood-cells.....	2700	3400	4150
Polymorphonuclears.....	43%	23%	9%
Small lymphocytes.....	47	59	85
Large lymphocytes.....	2	6	5
Large mononuclears.....	5	6	1
Transitionals.....	2	3	0
Eosinophils.....	1	1	0
Basophils.....	0	2	0

The red count and hemoglobin have been diminishing during her stay at the hospital, so that at present (6/26) the red blood-cells number 2,760,000; hemoglobin 40 per cent.

Blood-sugar (fasting), 98 mg. per 100 c.c. (0.98 per cent.). N. P. N.—28 mgm. Microscopic examination of an excised cervical lymph-gland by two pathologists showed a simple hyperplasia.

This case evidently belongs to the class of cases described by Mikulicz in 1892 and which has since been known as Mikulicz's disease or syndrome. It is quite a rare disease and is often associated with blood changes resembling leukemia; other cases seem closely allied to the lymphosarcomata. The disease in this case evidently began about January 1st at the time she had the epistaxis, as even at that time a leukopenia and relative increase in the lymphocytes were noted. It is evidently a progressive thing, and the course has been relatively acute. Some of the cases described under this heading have lived for years in comparatively good health aside from the disfigurement and a dryness of the mouth, while others terminate fatally in a short time. This case of Mikulicz's disease might perhaps be classed as a pseudoleukemia or possibly a lymphatic leukemia in the aleukemic stage. The induration of the skin which we see in this case has been described by von Bruns in a paper on this subject. This author also calls attention to the fact that in some of these cases there is no involvement of the lymphatic

glands or spleen and the blood-picture is normal, while in other cases there is a wide-spread enlargement of the lymph-glands



Fig. 285.—Notice indurated skin with sharp edge in temporal region and enlarged submaxillary gland.



Fig. 286.—Notice enlarged lacrimal gland causing drooping of eyelid, also enlarged parotid and submaxillary glands.

and moderate enlargement of the spleen. Occasionally the cases are associated with a severe anemia and aplasia of the

bone-marrow, while other cases terminate in a frank leukemia. Haeckel, quoted by Campbell Howard in an article in the "International Clinics" for 1909, described a case which closely resembled this one. A four-and-a-half-year-old girl had a symmetric enlargement of the lacrimal and salivary glands together with a general lymphatic enlargement. The blood-picture showed red blood-cells varying from 2,750,000 to 1,950,000; white blood-cells, 2600 to 1800; hemoglobin, 40 to 30 per cent., and differential count:

	Per cent.
Polymorphonuclears . . . . .	44.5-29.7
Small lymphocytes . . . . .	42 -65.6
Large lymphocytes . . . . .	1.7-10.0
Transitionals . . . . .	2 - 5.6
Large mononuclears . . . . .	0.3-10.4
Eosinophils . . . . .	0 0
Mast cells . . . . .	0 0

An occasional normoblast and a few megaloblasts were seen, as were also 1 or 2 megalocytes at one examination. The case improved temporarily under x-ray treatment, but succumbed to the disease after an illness of six months. He concluded that it was a case of pseudoleukemia with aplasia of the bone-marrow.

The prognosis of the cases that show no blood changes and no enlargement of the lymph-nodes is good aside from the disfigurement. In those showing blood and lymphatic changes the outlook is more serious, many of them dying in from six months to a year.

Practically nothing is known of the etiology, although Mikulicz thought it due to some parasite, while the treatment is entirely symptomatic; arsenic, iodid of potassium, and radium have been recommended. We tried a very light x-ray treatment of the one parotid in this patient, with the result of causing a sharp rise in the fever, but no improvement of the exposed part or in the general condition. In a few cases the enlargement of the lacrimals has been so extreme as to interfere with sight, due to inability to raise the upper eyelid. These cases have had the lacrimal glands removed, which entirely relieved this distressing feature.

**Subsequent Note.**—The patient left the hospital shortly after the above clinic was held, and I am informed that she died of a pulmonary hemorrhage on July 5th. There was no post-mortem. E. I. Bartlett, in the *Surgical Clinics of North America*, Vol. 3, No. 3, June, 1923, describes a case of Mikulicz's disease which improved very much after the introduction of radium needles into the enlarged glands.

## CLINIC OF DR. CHARLES HUGH NEILSON

ST. LOUIS UNIVERSITY

### FOCAL INFECTION IN GENERAL, WITH SPECIAL REFERENCE TO THE PROSTATE

THE subject of focal infection has been and is a topic about which a great deal has been written in recent years. It is of vital interest, but how much it has to do with secondary diseased conditions is still partly conjecture and partly real. Such men as Billings, Rosenow, Richet, Rosenau and Anderson, Hartzell, and others have given us many ideas on this important subject.

A study of focal infection and its causal relation to secondary diseased conditions has perhaps been overdone. The real thinkers and conservative men of the profession of medicine have not been overzealous, nor have they attributed all the ills of life to focal infection. Focal infection is often used as a diagnostic blanket which covers up carelessness, loose thinking, and many other clinical sins. The patients find it a real satisfactory explanation when perhaps there is no focal infection, or, if so, it causes no trouble. The needless sacrificing of teeth, the ruthless tonsillectomies, the multitude of sinus operations, etc., call for some conservatism by many dentists and physicians.

The list of diseases produced by focal infections includes nearly everything in the category of diseases. I do not wish to be understood as not believing in focal infection, but I do wish to emphasize the fact that we should be cautious, or else more thorough in our clinical investigations when focal infection may be a factor in the case.

Just what are focal infections? The term has come to mean more or less hidden infections where they are somewhat limited in their development by their position. This means that they are most often found in cavities where extension is difficult, for

example, in the roots of teeth, sinuses, gall-bladder, prostate, tubes, etc.

How are their effects produced? When we consider focal infection from this standpoint, we find that some few result in a direct extension to surrounding tissues. By far the greatest number produce metastatic infection through the lymph- and blood-stream. There is in all probability in many of these cases a decreased immunity to general infections through the slow and constant absorption of toxins. Direct toxic effects may produce pathologic changes, for example, arteriosclerosis. Another effect which seems probable is that in some cases there may be a sensitization produced by the absorption of bacterial substances, and perhaps by their direct toxins, which may cause some of the peculiar complaints of patients, complaints which often seem to have no pathologic basis for their explanation. These theoretic statements are difficult to prove clinically, but are clearly evident in some cases.

Has focal infection, as it has come to be understood, a symptomatology? For the sake of illustrating this point let us divide focal infections into two divisions:

1. Acute focal infections.
2. Chronic focal infections, which are really what the term "focal infection" means.

Acute focal infections, such as acute sinuses, tonsils, gall-bladders, appendicitis, tubes, prostates, etc., have a rather definite symptomatology, although subject to wide variations. Some of the symptoms are as follows:

1. Temperature is a rather constant symptom.
2. Pain is usually found and referable to the organ involved.
3. Rigors develop in many instances.
4. A leukocytosis in most cases is present.
5. There is usually a disturbance of function in the organ involved.

These definite and rather constant symptoms enable one with a proper study of the case to arrive at a definite diagnosis. Of course, there are often difficulties in so doing, but the end-result is usually an accurate diagnosis. All that is needed is



an accurate examination and accurate thinking, together with a rather definite symptomatology.

When we come to focal infection as understood by this term, the picture is entirely different. The effects of chronic focal infection sometimes invade surrounding tissues, but not often. The decreased immunity that it may produce is often incapable of being demonstrated. The anaphylactic symptoms are often a matter of conjecture. The metastatic effects are often more definite, but in many instances it is difficult to say positively.

Temperature is not an outstanding symptom. Pain is more often absent than present. Leukocytosis is usually absent. Disturbance of function is not a constant finding. The point which I wish to make here is that there is no clear-cut symptomatology in chronic focal infections, such as we find in acute focal infections. If there are no definite symptoms in these cases, how then can we make a diagnosis? This is done by its secondary effects, which are usually more definite than the ordinary constitutional effects of the infection.

What are some of the outstanding secondary effects by which we can assure ourselves that a given focus or foci are causing trouble? Every clinician who has had experience with these cases, I am sure, can recount many cases where a removal of a focus of infection has been followed by more or less relief from the symptoms. In some cases the secondary effects of a focal infection has advanced to such a point that removal of a focus does not show any definite result, and therefore one is not sure. I wish it understood that I believe in focal infection, but I wish again to emphasize the fact that we should be cautious, owing to the indefinite symptomatology and to the conjectural idea, that a given trouble may be due to a focal infection. How often can we say an endocarditis, myocarditis, and a pericarditis is due to a chronic focal infection? They are probably more often due to some acute focal infection or general infection. The chronic arthritides are perhaps more definite, but often here there is reason for doubt.

Arthritis deformans has been said to be due to focal infection. In some cases this is perfectly clear cut. In others we

know that in all probability the cause is a chemical one—whether the initial cause may have been a focal infection or not. How often we see these cases go merrily on their way even after many and sundry conjectural points of infection have been removed. Neuritis and focal infection have long been associated. In some cases there is a focus which causes the trouble. Its removal produces relief from the symptoms. Many cases are found where no focus can be found. Of course, the possibility remains that it may be overlooked, or the cause may be entirely different.

When we study cholecystitis, appendicitis, and gastric ulcer we think of focal infection. If Rosenow's theory is correct, many of these may be the end-results of focal infection elsewhere, which in time themselves become perhaps also points of focal infection. Multiple foci of infection often are found, such as teeth and gall-bladder, or appendix and gall-bladder, or tonsils and prostate, or sinus and teeth, etc. Is there a causal relation? It would seem so in some cases, but in many it is no doubt a coincidence.

The line of separation between the secondary results of a focal infection as now understood and the acute infections from some general infection is not sharp and clear cut. The secondary effects of focal infection is wide-spread if we include all diseases which have been attributed to such infection. In some cases the evidence is clear enough. In many it is not so clear. If we grant that metastatic infection is the most frequent effect of focal infection, we again have no definite symptomatology for focal infections. Surely the symptoms of each type of metastatic infection has its own symptomatology. Chronic arthritis, arthritis deformans, spondylitis, neuritis, lumbosacral disease, myositis, each have a set of symptoms which is peculiar to itself and not due to the focal infection. If we should go through the list of possible metastatic focal results, the same conclusion must be reached. This fact, coupled with the rather indefinite general results as above described, causes us to conclude that chronic focal infection has no definite symptomatology. As an aid to its diagnosis we must rely on effects, which may or

may not be direct end-results. We, therefore, are bound in many instances to have only a conjectural connection between cause and effect.

The idea of focal infection has certainly had a far-reaching result in causing clinicians to hunt far and wide for a focus of infection in many diseases possibly so related. The sites of the initial focal infection which are most common, as we all know, are the accessory nasal sinuses, the teeth, and the tonsils. At least such trouble is produced by infection at these sites. We must not limit focal infection to these points. The gall-bladder, the appendix, the kidney and its pelvis, the tubes, the prostate, the rectum and rectosigmoid, and often the lymph-glands are frequent foci of infection.

They may have become secondarily infected, but are often the initial focal infection in a given case.

In this discussion I wish to call your attention to the prostate as a frequent focus of infection. The genito-urinary specialist has long studied this condition. He has, however, given more attention to it entirely from the standpoint of a local infection, both acute and chronic. He does not often consider it as a focus of infection, which often causes secondary effects. I feel sure the prostate is probably one of the most frequent sites of focal infection in men.

In my office practice a study of the prostate has been carried on, and the results are startling. It has always been the custom of internists to palpate the prostate, but it is not their custom, at least generally, to massage and study the prostatic secretion. I have carried this out in over 200 men who came to me for examination and diagnosis. These men did not come for a diagnosis of their prostatic troubles, but for conditions which naturally fall to all internists. Many of these men had been repeatedly examined, but the prostate had never been touched. Many of them had been through the hands of some of our great diagnostic teams, and this examination had been neglected. In this study of these prostates, as a point of focal infection, there were no acute cases, and none were tabulated in any results who had had a Neisser infection under two years preceding the

examination. I did not pick special cases, but examined and tabulated the results on every case who came to my office for an examination.

I might remark at this point that I have examined the clinical records in a large hospital and found a very complete and a careful set of records, but there were only a few cases where the prostate had been examined, and these were for some acute prostatic trouble. It is also a surprising fact how little information one can find in text-books concerning chronic infections of the prostate. Hypertrophy of the prostate and its effects are well described, but not chronic infections of the prostate.

In my examination of the prostatic fluid all precautions were taken to avoid any infectious material from urethra and outside infection. The prostatic fluid was studied in two ways. A drop was placed on a slide and covered. A study of the leukocyte count was made, and also it was noted whether any bacteria could be found. A smear was also made, and this was stained by methylene-blue, and the number of leukocytes and bacteria was noted. In many cases great numbers of leukocytes are found with no bacteria. In others not so many leukocytes and many bacteria. In fact, all combinations have been made and some difficulties have been found. If there was any doubt as to a real definite infection in a given case, this was not tabulated as an infected prostate. In another paper I am giving my results, my methods, and my difficulties more in detail.

It is sufficient for this discussion to study the results. Of the 200 examinations, 85 had clearly infected prostates. This seems a large percentage, and this is a startling fact when we come to consider the incidence of focal infection in other sites. Of these 85 infected prostates, 58 had a history of a Neisser infection from two to forty years previously. I question whether any one who has had gonorrhea ever entirely escapes a prostatic infection. The relation of prostatic infection to prostatic hypertrophy is an interesting question. It does not belong in this discussion, but I cannot refrain from mentioning it.

A classification of these cases with infected prostates is as follows:

Nine had lumbar and sacral spondylitis, and came for treatment for lame backs.

Fifteen had lumbago, or sacro-iliac disease, where no evidence of other secondary infection was found.

Seven came for nervousness and rapid heart. Three of these had infected tonsils in addition.

One was sent by an oculist. The patient had an iritis.

The worst possible prostate was found as the only cause of focal infection. He had been examined by two other internists and the prostate had not been examined. Three were diagnosed as prepyloric gastric ulcers. Whether the condition of the prostate had any influence on the causation of the ulcer is questionable.

Three had duodenal ulcers, but very bad prostates.

Six came for weakness of sexual power. The ages of these men were from thirty-five to forty-three. In these cases the prostates were found badly infected and, in addition, there was marked prostatic hypertrophy.

Two had had vigorous endocrine treatment, but no prostatic examination. It is said by genito-urinary specialists that prostatic trouble of this kind is the most frequent cause of early loss of sexual vigor. One was a case of early senility in a man fifty-three. He had a badly infected and hypertrophied prostate with all senile changes very marked. Sexual vigor was lost at forty.

One had spurs on the os calcis of both feet.

Four had sciatic rheumatism.

Five came for rheumatism, which was not the trouble, but, in all probability, was a neuritis.

One with similar symptoms was a subdeltoid bursitis.

Four had pulmonary tuberculosis, but had clear-cut prostatic infection. All had had gonorrhea. They were sent to the city for diagnosis. In only one case was there a suspicion of the tuberculosis, and in none had the prostate been examined.

Fifteen came for diagnosis, as to why they were nervous, losing weight, together with aching of the bones, and a constant catching of colds. Were their prostates responsible? I have no doubt that the infected prostates were at least partly

responsible. Massage of prostate with other appropriate treatment has materially benefited part of them. How much should be attributed to the prostatic treatment I do not know.

Two were diagnosed sexual neurasthenics of the worst sort. They had the symptoms, such as fear of sexual impotence, etc.

Four were diagnosed as general neurasthenics of the worst sort. They had the physical fears, the so-called indigestions, the fatigue states, etc.

Five had so-called chronic rheumatism, with stiffened joints at times. In three of these there were occasional subacute attacks, with some redness and swelling. One of these had a beginning arthritis deformans, and one other seemed more like gouty attacks than a rheumatism. In one of these cases a culture of the prostatic secretion showed a streptococcus in almost pure culture.

No attempt has been made in this discussion to give results of treatment, partly because many were sent back to their physician and prostatic treatment was not carried out, or, if so, only indifferently. Some were lost sight of. Some refused treatment. In some it is too early to state whether any effect has been obtained. Some results, as above mentioned, have been quite conclusive in the group of sacro-iliacs and lumbagos. Prostatic treatment with other appropriate treatment has apparently yielded good results. It is always difficult in focal infections to state how much good results from removal of the focus. It is especially so in prostatic focal infection for the same reason, and also the added difficulty that getting rid of the prostatic infection is difficult and often next to impossible.

**Conclusions.**—A study of focal infections in general has led me to formulate the statement that there is no recognized set of symptoms. The symptoms found are the individual symptoms of each type of secondary effects.

A study of the prostate from the standpoint of the internists leads me to state that the average physician and many internists have neglected the prostate in their search for focal infection. I believe the prostate is perhaps the most frequent cause of focal infection in men.

